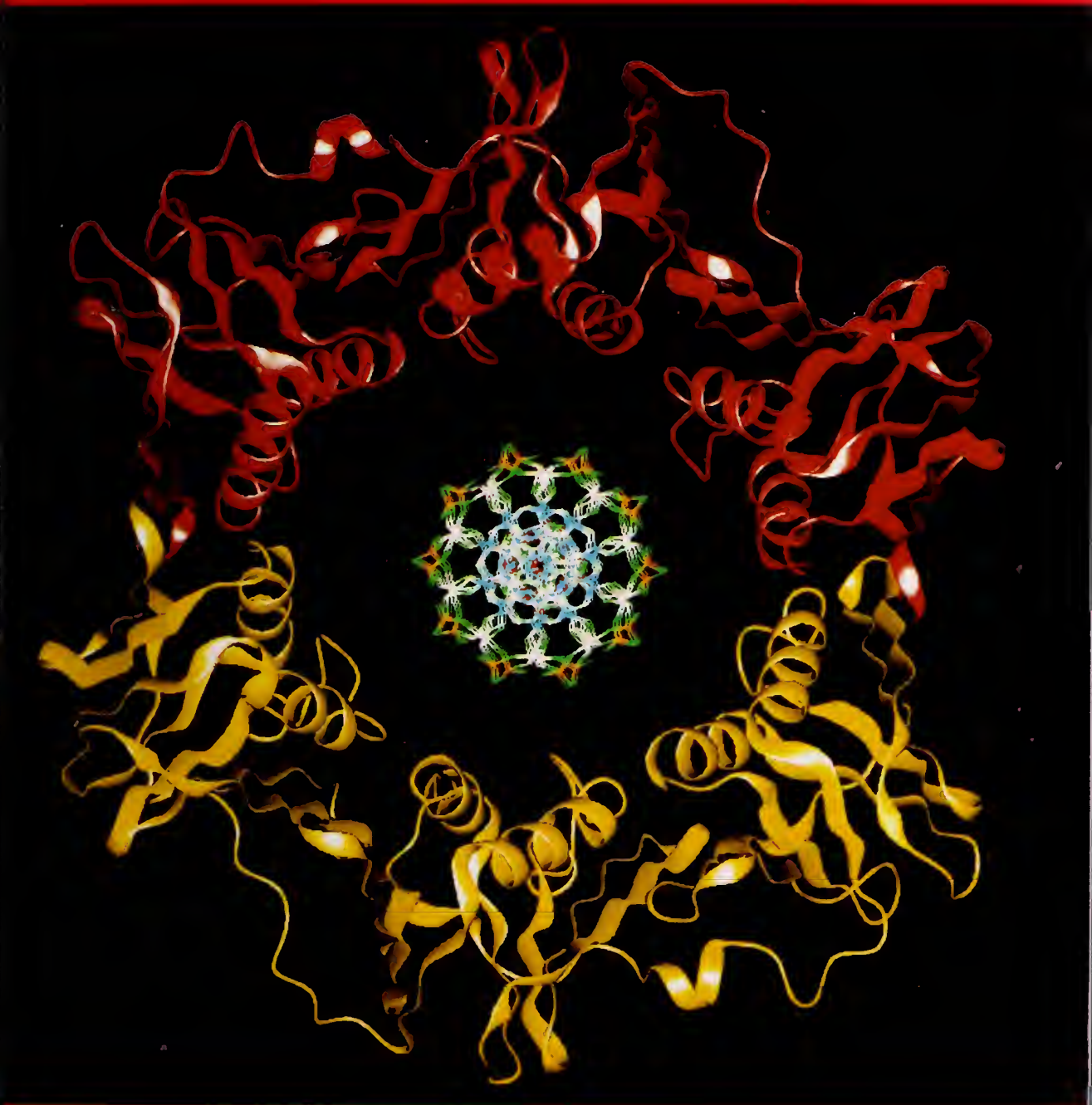
Cornell University
Graduate School of Medical Sciences



Catalog 1994–1995

Academic Calendar 1994–95

1994

Orientation for new students	Wednesday, August 24–Thursday, August 25
Opening Exercises	Wednesday, August 24
Registration for **Quarter I*** and **Fall semester****	Wednesday, August 24–Friday, August 26
Quarter I and **Fall semester** begin	Monday, August 29
Labor Day Holiday observed	Monday, September 5
Quarter I ends	Friday, October 21
Examinations for **Quarter I**	Friday, October 21–Friday, October 28
Registration for **Quarter II***	Friday, October 28 and Monday, October 31
Quarter II begins	Monday, October 31
Thanksgiving recess	Thursday and Friday, November 24 and 25
Winter recess: Instruction suspended 5:00 p.m.	Friday, December 16

1995

Winter recess ends: Instruction resumed 9:00 a.m.	Tuesday, January 3
Quarter II and **Fall semester** end	Wednesday, January 11
Last day for completing requirements for January degrees	Friday, January 13
Conferral of January degrees	Wednesday, January 18
Examinations for **Quarter II**	Thursday, January 12–Friday, January 20
Martin Luther King, Jr.'s Birthday observed	Monday, January 16
Registration for **Quarter III*** and **Spring semester*****	Friday, January 20 and Monday, January 23
Quarter III and **Spring semester** begin	Monday, January 23
Presidents' Day Holiday observed	Monday, February 20
Last day for registering for participation in Commencement	Friday, February 24
Quarter III ends	Friday, March 17
Examinations for **Quarter III**	Monday, March 20–Friday, March 24
Spring recess	Monday, March 27–Friday, March 31
Registration for **Quarter IV**	Friday, March 31 and Monday, April 3
Quarter IV begins	Monday, April 3
Fifteenth Annual Vincent duVigneaud Memorial Research Symposium; no classes	Thursday, May 4
Last day for completing requirements for May degrees	Friday, May 19
Commencement Day, conferral of May degrees, 3:00 p.m., Avery Fisher Hall	Thursday, May 25
Quarter IV and **Spring semester** end	Friday, May 26
Memorial Day Holiday observed	Monday, May 29
Examinations for **Quarter IV**	Tuesday, May 30–Friday, June 2

Summer Term 1995

Summer research term begins	Monday, July 3
Independence Day holiday observed	Tuesday, July 4
Last day for completing requirements for August degrees	Friday, August 25
Conferral of August degrees	Monday, August 28
Summer research term ends	Tuesday, August 29

Fall Semester 1995 (Projected)

Orientation for new students	Wednesday, August 23–Thursday, August 24
Opening Exercises	Wednesday, August 23
Registration for **Quarter I*** and **Fall semester****	Thursday, August 24–Friday, August 25
Quarter I and **Fall semester** begin	Monday, August 28
Labor Day Holiday observed	Monday, September 4

* for students enrolling in courses.

** for students conducting research only, who are on leave of absence, or who are *in absentia.*

*** for students changing from course work to research, who are going on leave of absence, or who are converting to *in absentia* status.

Note: Courses are taught on a quarterly basis, degrees are granted at ends of the Fall and Spring semesters and of the summer term. The dates shown in the calendar are subject to change at any time by official action of Cornell University.

In enacting this calendar, the Graduate School of Medical Sciences has scheduled classes on religious holidays. It is the intent of the school that students missing classes due to the observance of religious holidays be given ample opportunity to make up work.

Cornell University

Graduate School of Medical Sciences 1994 • 1995

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On the cover:
The β subunit of *E. coli* DNA polymerase III holoenzyme is a dimer in the shape of a ring. The β ring completely encircles DNA (center) and acts as a "DNA sliding clamp" to tether the polymerase machinery down to DNA for highly processive DNA synthesis. From the laboratories of Dr. Michael O'Donnell and his associates (*Cell* 69:425–437, 1992).

Editor/Coordinator: Carolyn B. Schnall

Contents

The courses and curricula described in this Catalog, and the teaching personnel listed herein, are as of July 1, 1994 and are subject to change at any time by official action of the Cornell University Graduate School of Medical Sciences.

New York Hospital-Cornell Medical Center (background, right of center), Memorial Sloan-Kettering Cancer Center (left), and The Rockefeller University (foreground), on Manhattan's East Side

Cornell University
Graduate School of Medical Sciences

Purpose

The Graduate School of Medical Sciences, a semi-autonomous component of the Graduate School of Cornell University, provides opportunities for advanced study and research training in specific areas of the biomedical sciences. Graduate training leading to the degree of Doctor of Philosophy is offered by the following programs of study: *Biochemistry and Structural Biology, Cell Biology and Genetics, Immunology, Molecular Biology, Neuroscience, Pharmacology, and Physiology and Biophysics.* The *Interdisciplinary Program in Molecular and Cellular Biology* admits students "at large", i.e., without initial commitment to one of the above programs. Under special circumstances, students may also be admitted as Master of Science candidates. Collaborative programs with Cornell University Medical College lead to the combined degrees of Doctor of Philosophy and Doctor of Medicine.

The faculty of the Graduate School of Medical Sciences recommends the award of advanced general degrees not only as the result of the fulfillment of certain formal academic requirements, but also as evidence of the development and possession of a critical and creative ability in science. Demonstration of this ability is embodied in a dissertation which the candidate presents to the faculty as an original research contribution in the chosen area of study.

A close working relationship between student and faculty is essential to the program of the Cornell University Graduate School of Medical Sciences. Guidance for each student is provided by a Special Committee, a group of at least three faculty members selected by the student. This Special Committee is granted extraordinary independence in working with its student. Other than a broad framework of Graduate School of Medical Sciences requirements for residence, examinations, and a thesis, and additional requirements of the particular field of study chosen by the student, the Special Committee is free to design an individualized program of study with its students. No overall course, credit-hour, or grade requirements are set by the Graduate School of Medical Sciences. A student is recommended for a degree whenever the Special Committee judges the student qualified.

History

The opportunity for graduate study leading to advanced general degrees in the biomedical sciences was first offered at the Cornell University Medical College, in cooperation with the Graduate School of Cornell University, in 1912. In June of 1950, Cornell University, in association with the Sloan-Kettering Institute for Cancer Research, established additional opportunities for graduate study by forming the Sloan-Kettering Division of the Medical College. The resulting expansion of both graduate faculty and research training opportunities on the New York City campus prompted the organization in January, 1952 of the Graduate School of Medical Sciences, composed of two cooperative but separate divisions, known as the Medical College Division and the Sloan-Kettering Division. The Graduate School of Medical Sciences was given full responsibility for advanced general degrees granted for study in residence on the New York City campus of Cornell University.

Facilities

The Cornell University Graduate School of Medical Sciences is part of a large biomedical center extending along York Avenue between 65th and 72nd Streets on Manhattan's East Side. This complex includes Cornell University Medical College, New York Hospital, the Memorial Sloan-Kettering Cancer Center, and The Rockefeller University. The core facilities of the Graduate School of Medical Sciences, which include the research laboratories of its faculty, are located within the Cornell Medical College—New York Hospital complex and the Howard, Kettering, Rockefeller, and Schwartz Laboratory buildings of the Sloan-Kettering Institute for Cancer Research. Other buildings in this area provide student housing and recreational facilities. Several dining rooms and snack bars are located in this complex, and the immediate neighborhood abounds in a large variety of restaurants.

Especially noteworthy are two large biomedical libraries available to graduate students. The smaller of the two, the Medical Library—Nathan Cummings Center, contains over 32,700 books and journals. The Cornell University Medical College Library has a collection of 151,000 volumes and subscriptions to 1,400 journals. It is one of the country's first fully automated medical libraries featuring computer terminals which provide access to library materials and permit bibliographic searches in a number of data bases. A microcomputer center, with an extensive software collection, is maintained at the library for staff and students.

Organization

The faculty of the Graduate School of Medical Sciences is composed of the professional staffs of the basic science and clinical departments of Cornell University Medical College, and the professional staff members of the Sloan-Kettering Institute for Cancer Research.

Graduate training is offered in several areas of the biomedical sciences. These Programs of Study bring together faculty members who have related research and teaching interests.

Executive Committee

The Executive Committee is both the administrative and judicial board of the Graduate School of Medical Sciences and its members have continuing responsibility for the academic affairs of the school. The Committee is composed of the Chairpersons of the graduate programs, the Dean as chairperson, the Associate Dean, the Provost for Medical Affairs of Cornell University, the Chairperson or Vice-Chairperson of the Sloan-Kettering Institute, the Chairperson and Vice-Chairperson of the Faculty Advisory Committee (see below), and two non-voting, elected student representatives.

The Executive Committee considers such matters involving the interests and policies of the Graduate School of Medical Sciences as are referred to it by the Faculty Advisory Committee, by individual members of the Faculty, or are generated upon its own initiative. The Committee approves the addition or deletion of

programs of study, reviews the admission of students, approves a student's major and minor programs, reviews the curriculum and requirements for degrees.

The Executive Committee is chaired by the Dean, who is the academic administrative officer of the Graduate School of Medical Sciences and is also an Associate Dean of the Graduate School of Cornell University. The Associate Dean, who is also an Assistant Dean of the Graduate School of Cornell University, is the Secretary of the Executive Committee.

Faculty Advisory Committee

The Faculty Advisory Committee is the primary body representing the views of the Faculty of the Graduate School of Medical Sciences. The Committee advises the Dean and the Executive Committee on the impact of educational and policy matters under their consideration and recommends changes in educational activities, procedures, and policy of the Graduate School of Medical Sciences.

The Faculty Advisory Committee is composed of the elected Program Directors and two elected student representatives. The Chairperson and Vice-Chairperson of the Committee are elected by its membership. Non-voting members are the Dean and Associate Dean, the Provost for Medical Affairs of Cornell University, and the Chairperson or Vice-Chairperson of the Sloan-Kettering Institute.

Special Programs

Tri-Institutional MD-PhD Program

This program offers a small number of highly qualified college graduates the opportunity to study both clinical and biomedical disciplines leading to the MD and PhD degrees. The combination of basic research skills and clinical experience prepares students in the program for teaching and investigative careers. Preclinical and clinical training are provided by the faculty of Cornell University Medical College. Research opportunities are offered in the laboratories of the Cornell University Graduate School of Medical Sciences, The Rockefeller University, and the Sloan-Kettering Institute.

The MD-PhD Program offers an intensive and intellectually challenging six-to-seven-year course of study. Participants spend the first two years as medical students mastering the preclinical sciences and attending research-oriented seminars led by experts in the biomedical fields. The summer months are spent in the laboratory learning experimental techniques and doing research. The students spend the next three to four years as full-time graduate students, mainly doing laboratory research and writing the thesis. Research training is offered in the following areas: biochemistry, cell and developmental biology, immunology, molecular biology and genetics, molecular pharmacology and therapeutics, neuroscience, physiology and biophysics, and virology and microbiology. The final year consists of required clerkships in medicine, surgery, obstetrics and gynecology, pediatrics, neurology, psychiatry, radiology, public health, and anesthesiology. The six-to-seven-year plan satisfies the minimum residency requirements for both the MD and PhD degrees.

A successful applicant will demonstrate excellent undergraduate science preparation and a strong commitment to combining an investigative career in the biomedical sciences with clinical medicine. Applicants must satisfy the requirements of each institution. All students accepted in the MD-PhD Program receive full-tuition scholarships and stipends to cover living expenses for the entire period.

For application to the MD-PhD Program, see p. 71.

PhD-MD Program

Students enrolled in the Graduate School of Medical Sciences may be eligible for admission into the PhD-MD Program, jointly sponsored by the Medical College and the Graduate School of Medical Sciences. This program is designed for those graduate students who find that their teaching and research goals require the acquisition of the MD degree in addition to the PhD degree. The program is *not* designed as an alternate path for students who have the MD degree as their primary goal, but who have not been accepted by a medical school. Those who know, at the time of application to Cornell, that they want to pursue a course of study leading to both degrees should apply to the MD-PhD program described above.

See p. 72 for application and graduation requirements of the PhD-MD program.

Faculty and Research Activities

Program in Biochemistry and Structural Biology

Faculty

Esther M. Breslow
David P. Hajjar
Franz-Ulrich Hartl
Jerard Hurwitz
Richard N. Kolesnick
Kenneth J. Marians
Michael E. O'Donnell
Dinshaw J. Patel
Nikola P. Pavletich
Marilyn D. Resh
Hugh D. Robertson
James E. Rothman
Stewart Shuman
Paul Tempst

Research Activities

Members of the Biochemistry and Structural Biology program are engaged in research spanning a wide spectrum of scientific areas in which a variety of modern techniques of molecular biology and chemistry is used.

Dr. Breslow is concerned with understanding the forces that determine the specificity of protein-protein interactions and the relationship between protein structure and function. Her laboratory has focused on the interactions of the pituitary peptide hormones, oxytocin and vasopressin, with their storage protein, neurophysin, as a model system for these investigations. The relationship of mutations in neurophysin to the disease diabetes *insipidus,* in which vasopressin secretion is impaired, also makes this a useful model to study the molecular basis of a disease process. Recent studies have led to the elucidation of the first X-ray crystal structure of a neurophysin complex. Present work is focused on determining the mechanism by which the hormones guide the folding of the neurophysin chain, on the application of molecular mechanics to the analysis of binding specificity by the neurophysins, and on the molecular mechanism by which the binding of hormones to neurophysin influences its allosteric properties.

Dr. Hajjar's laboratory is committed to defining the role of specific signal transduction mechanisms in the control of cholesterol trafficking via LDL and scavenger receptors. Opportunities are available for students to work on projects which focus on the study of the interactions of growth factor (FGF, PDGF) and cytokine (IL-1) receptors with the LDL receptor, how this receptor coupling impacts on LDL receptor conformation, transcription and expression, and the mechanisms by which the eicosanoid and cytokine network are linked to regulate cholesterol trafficking.

The role of molecular chaperones in catalyzing the folding of newly synthesized polypeptides is the major focus of *Dr. Hartl's* research. How members of the hsp70 and hsp60 families direct protein folding and intracellular sorting is of specific interest.

Dr. Hurwitz's group studies the enzymes and enzymological processes involved in mRNA splicing in human cells. His laboratory uses the adeno and SV40 viral DNA replication systems as probes for the enzymatic mechanisms of cellular DNA replication.

Dr. Kolesnick's research program focuses on the role of complex lipids in several signal transduction pathways. He has identified a new signal transduction pathway, termed the sphingomyelin pathway, which mediates the action of cytokines such as tumor necrosis factor (TNF)α and interleukin-1 (IL-1)β. Research opportunities exist in

his laboratory to further define the relationship between activation of the sphingomyelin pathway and TNF signal transduction systems in a variety of cell types.

Dr. Marians focuses on studies of the enzymological mechanisms of DNA replication in *Escherichia coli,* using cell-free systems. The use of *in vitro* DNA replication systems composed of purified replication proteins enables detailed analyses of the interaction of the replication proteins with each other and with the DNA template. The role of topology in DNA replication, as well as the mechanisms of DNA topoisomerases, is also under study in his lab.

A detailed examination of the molecular mechanics of DNA replication is the focus of *Dr. O'Donnell's* laboratory. The dynamic motions on templates of the multi-protein replicative polymerase of *E. coli* and its interaction with other proteins at the replication fork are under study. Dr. O'Donnell is also investigating the control of replication initiation in Epstein-Barr virus.

Dr. Patel's laboratory focuses on the combined application of Nuclear Magnetic Resonance (NMR) and Molecular Dynamics (MD) calculations to determine the solution structure of higher order nucleic acids, covalent carcinogen-DNA adducts and antitumor drug-DNA complexes. The major effort in the area of *higher order nucleic acid structures* has focused on DNA triplexes and quadruplexes. Research opportunities exist to identify those factors (hydrogen bonding, base stacking, metal cation dependence, glycosidic torsion angles, strand directionality) that define base triple and quadruple alignments and the characterization of the structural realignments needed to accommodate non-standard pairings within DNA triplexes and quadruplexes. Future efforts will address potential cross-talk between ligands positioned within the different grooves of these higher order nucleic acid structures.

Dr. Pavletich's laboratory is interested in understanding the structural basis of oncogene and tumor suppressor function. Current research is aimed at obtaining high resolution structural information about the p53 tumor suppressor system by x-ray diffraction methods. p53 plays a critical role in preventing cancer, and its inactivation through missense mutations is the most frequently observed genetic alteration in human cancers (occurring in about half of all cases). Mutations result in loss of sequence specific DNA-binding activity, consistent with this activity playing a critical role in preventing tumorigenesis. Towards understanding how p53 is inactivated, his group has recently determined the crystal structure of a p53-DNA complex. The crystal structure reveals how p53 binds DNA and suggests possible targets for the design of compounds to restore activity to p53 mutants.

Dr. Resh's research concerns the molecular mechanism of cellular transformation by RNA tumor viruses. The long term objective is to understand how oncoproteins associate with cellular membranes and why membrane interaction is important for transformation. The focus is on the transforming gene product of Rous sarcoma virus, $pp60^{v\text{-}src}$, a myristylated, membrane-bound tyrosine protein kinase. Attachment of myristylated $pp60^{v\text{-}src}$ to the plasma membrane is essential for expression of the oncogenic phenotype. During the past several years, this laboratory has established novel *in vitro* systems to study the biosynthesis, fatty acylation and membrane insertion of $pp60^{v\text{-}src}$. The molecular basis for association of $pp60^{v\text{-}src}$ and related Src family members with membranes has been defined. Current work is concentrated on the enzymology of protein fatty acylation reactions.

Dr. Robertson's research employs structural probes for the analysis of biologically active RNA molecules. Techniques of direct RNA sequencing; binding of proteins which recognize double-stranded RNA; and UV-induced RNA-RNA crosslinking are applied to analysis of ribozymes and other critical sites in delta hepatitis agent RNA and other self-replicating RNAs.

The work in *Dr. Rothman's* laboratory is focused on intracellular protein sorting. An *in vitro* transport system derived from Golgi stacks has been developed; this system allows a biochemical analysis of protein sorting and the associated protein modifications. Biochemical analysis of one factor (NSF) essential for the transport process is under way.

Both biochemical and genetic aspects of transcriptional control, with particular emphasis on transcription termination in purified *in vitro* systems, are under study by Dr. Shuman using vaccinia virus as a model.

Dr. Tempst's laboratory studies the activities and regulation of antimicrobial peptides, which are major components of insect and mammalian innate immune systems. Prospects of clinical applications are being evaluated. The laboratory is also developing high resolution chromatographic and electrophoretic techniques, and high sensitivity protein sequencing methods and instrumentation to investigate various cellular events at the protein level. Applications include protein interactions and modifications.

Recent Publications

Breslow, E. (with Huang, H.-B.), Identification of the unstable neurophysin disulfide and localization to the hormone-binding site: relationship to folding pathways. *J. Biol. Chem.* 267:6750–6756, 1992.

Breslow, E. (with Mishra, P. K., Huang, H.-B., and Bothner-by, A.), Slowly interchanging conformers of bovine neurophysin-I in the unliganded dimeric state. *Biochemistry* 31:11397–11404, 1992.

Breslow, E. (with Huang, H.-B. and LaBorde, T.), Modulation of allosteric interactions in neurophysin induced by succinylation of serine-56 of cleavage of residues 1–8. *Biochemistry* 32: 10743-10749, 1993.

Hajjar, D. P. (with Pomerantz, K. B.), Molecular motions and thermotrophic phase behavior of cholesterylesters: a deuteron nuclear magnetic resonance (NMR) spectroscopy study. *Biophysical Chemistry* 43:255–263, 1992.

Hajjar, D. P. (with Pomerantz, K. B.), Elcosanoid metabolism in cholesterol-enriched arterial smooth muscle cells. Evidence for reduced post-transcriptional processing of cyclooxygenase 1 and reduced cyclooxygenase II gene expression. *Biochemistry* 32: 13824–13835, 1993.

Hajjar, D.P. (with Heu, H. Y. and Nicholson, A. C.), Basic FGF-induced LDL receptor transcription and surface expression: signal transduction pathways mediated by FGF receptor tyrosine and protein kinases. *Journal of Biological Chemistry* 269:9213–9220, 1994.

Hartl, F-U. (with Frydman, J., Nimmesgern, E., Erdjument-Bromage, H., Wall, J. S., and Tempst, P.), Function in protein folding of TRIC, a cylosolic ring-complex containing TCP-1 and structurally-related subunits. *EMBO J.* 11:4767–4778, 1992.

Hartl, F-U. (with Martin, J., Mayhew, M., and Langer, T.), The reaction cycle of GroEL and GroES in chaperonin-assisted protein folding. *Nature* 366:228–233, 1993.

Hurwitz, J. (with Stigger, E., Dean, F., and Lee, S.-H.), Reconstitution of functional human single-shaded DNA-binding protein from individual subunits expressed by recombinant baculoviruses. *Proc. Natl. Acad. Sci., USA* 91:579–583, 1994.

Hurwitz, J. (with Amin, A. A. and Murakami, Y.), Initiation of DNA replication by simian virus 40T antigen is inhibited by the p107 protein. *J. Biol. Chem.* 269:7735–7743, 1994.

Kolesnick, R. N. (with Mathias, S., Younes, A., Kan, C., Orlow, I., and Joseph C.), Activation of the sphingomyelin signaling pathway in intact EL4 cells and in a cell-free system by IL-1β. *Science* 259:519–522, 1993.

Kolesnick, R. N. (with Golde, D. W.), The sphingomyelin pathway in tumor necrosis factor and interleukin-1 signaling. *Cell* 77:325–328, 1994.

Marians, K. J. (with Tougu, K. and Peng, H.), Identification of a domain of *Escherichia coli* primase required for functional interaction with the DnaB Helicase on the replication fork. *J. Biol. Chem.* 269:4675–4682, 1994.

Marians, K. J. (with Hiasa, H.), Primase couples leading- and lagging-strand DNA synthesis from *oriC*. *J. Biol. Chem.* 269:6058-6063, 1994.

O'Donnell, M. E. (with Stukenberg, T., and Studwell, P. S.), Mechanism of the sliding β-clamp of DNA Polymerase III Holoenzyme. *J. Biol. Chem.* 266:11328-11334, 1991.

O'Donnell, M. E. (with Kong, X.-P., Onrust, R., and Kuriyan, J.), Three-dimensional structure of the β subunit of *E. Coli* DNA Polymerase III Holoenzyme: a sliding DNA clamp. *Cell.* 69:425-437, 1992.

Patel, D. J. (with Radhakrishnan, I.), Solution structure of a purine-purine-pyrimidine DNA triplex containing G-GC and T-AT triples. *Structure* 1:135-152, 1993.

Patel, D. J. (with Wang, Y.), Solution structure of the human telomeric repeat $d(AG_3[T_2AG_3]_3)$ G-tetraplex. *Structure* 1:263-282, 1993.

Pavletich, N. P. (with Chambers, K. and Pabo, C.O.), The DNA binding domain of p53 contains the four conserved regions and the major mutation hotspots. *Genes and Development* 7:2556-2564, 1993.

Pavletich, N. P. (with Cho, Y., Gorina, S., and Jeffrey, P.D.), Crystal structure of a p53 tumor suppressor-DNA complex: Understanding tumorigenic mutations. *Science* 265:346-355, 1994.

Resh, M. D., Myristylation and palmitylation of src family members: The fats of the matter. *Cell* 76:411-413, 1994.

Resh, M. D. (with Berthiaume, L., Deichaite, I., and Peseckis, S. M.), Regulation of enzymatic activity by active site acylation: A new role for long chain fatty acid acylation of proteins. *J. Biol. Chem.* 269:6498-6505, 1994.

Robertson, H. D. (with Branch, A. D.), Comparative ribozyme structure and function of delta agent RNA and RNA of other circular subviral RNA pathogens. In: J. Taylor, F. Bonino, and S. Hadziyannis eds., *Hepatitis Delta Virus: Molecular Biology, Pathogenesis, and Clinical Aspects,* Wiley-Liss, N.Y., pp. 79-88, 1993.

Robertson, H. D. (with Branch, A. D., Lee, S. E., and Neel, O. D.), Prominent polypurine and polypyrimidine tracts in plant viroids and in RNA of the human hepatitis delta agent. *Nucleic Acids Res.* 21:3529-3535, 1993.

Rothman, J. E. (with Sollner, T., Whiteheart, S. W., Brunner, M., Erdjument-Bromage, H., Geromanos, S., and Tempst, P.), SNAREs, SNAP receptors implicated in vesicle targeting and fusion. *Nature* 362:318-324, 1993.

Rothman, J. E. (with Ostermann, J., Orci, L., Tani, K., Amherdt, M., and Ravazzola, M.), Stepwise assembly of functionally active transport vesicles. *Cell* 75:1015-1025, 1993.

Shuman, S. (with Hagler, J. and Luo, Y.), Mechanism of factor-dependent transcription termination by vaccinia RNA polymerase; Kinetic coupling and requirement for ATP hydrolysis. *J. Biol. Chem.* (in press), 1994.

Shuman, S. (with Schwer, B.), Mutational analysis of yeast mRNA capping enzyme. *Proc. Natl. Acad. Sci., USA* (in press), 1994.

Tempst, P. (with Casteels, P., Ampe, C., and Jacobs, F.), Functional and chemical characterization of hymenoptaecin, an inducible antibacterial polypeptide in the honeybee *(Apis mellifera)*. *J. Biol. Chem.* 268:7044-7054, 1993.

Tempst, P. (with Casteels-Josson, K., Capeci, T., and Casteels, P.), *Apidaecin* multipeptide precursor structure: a putative mechanism for amplification of the insect antibacterial response. *EMBO J.* 12:1569-1578, 1993.

Program in Cell Biology and Genetics

Faculty

Rosemary F. Bachvarova
David Bader
Robert Benezra
Carl P. Blobel
Anthony M. C. Brown
Michael A. Caudy
Raju S. K. Chaganti
Moses V. Chao
Jacques Cohen
Donald A. Fischman
Leonard P. Freedman
James L. German, III
Marvin C. Gershengorn
Barry M. Gumbiner
David P. Hajjar
Franz-Ulrich Hartl
Eric A. Jaffe
Maria Jasin
Irwin L. Klein
Eseng Lai
Paul A. Marks
Joan Massague
Takashi Mikawa
Malcolm A. S. Moore
Ralph L. Nachman
Carl F. Nathan
Joel D. Pardee
Marilyn D. Resh
Richard A. Rifkind
Hugh D. Robertson
Enrique Rodriguez-Boulan
Neal Rosen
James E. Rothman
Roy L. Silverstein
Martin Sonenberg
Lisa Staiano-Coico
Paula Traktman
John A. Wagner
Martin Wiedmann
David Zakim

The faculty of the Program in Cell Biology and Genetics conducts research in a broad range of fields that includes the most exciting areas of genetics and cell-developmental and molecular biology. Specific interests include the developmental biology of the early embryo and of cardiovascular and muscle tissues; membrane biology, cell motility and the cytoskeleton; the molecular biology of cell growth, differentiation, and oncogenic transformation; endocrinology and hormone receptors; human somatic cell and cytogenetics; and molecular virology. These studies are pursued employing the most current cell biological, genetics, molecular, and immunological techniques and methodologies in modern and well-equipped facilities.

Research Activities

The following comprise brief detailed descriptions of faculty research and the scope of study in the program.

Dr. Bachvarova is interested in the steps leading up to gastrulation in the mouse embryo. Current projects include analyses of the effects of growth factors on cultured mouse embryos and the expression of growth factors, their receptors, and early-response transcription factors that may be involved in mesoderm induction.

Dr. Bader's laboratory is concerned with the commitment and differentiation of cardiac progenitor cells. The cellular and molecular controls of cardiac gene expression are of central interest.

Dr. Benezra's research is focused on the newly discovered *Id* protein, a functional antagonist of the helix-loop-helix class of transcriptional activators. His interest is the role of this transcriptional repressor in embryonic development and muscle differentiation.

Dr. Blobel's lab is studying the role of a new family of integrin ligands in fertilization and myogenesis. This new protein family is related to the snake venom integrin ligands called disintegrins, and is implicated in cell-cell binding fusion and potentially in signaling.

Dr. Brown's laboratory is studying the family of *Wnt* genes, which encodes intercellular signaling molecules that function in both embryogenesis and tumorigenesis. A major focus is the protein product of the proto-oncogene *Wnt-1* and its mechanism of action in cell culture systems.

Dr. Caudy is interested in the molecular genetic mechanisms which control neuronal pattern formation during development. A network of cell determination genes that controls neuronal cell fate in *Drosophila* embryos are the major focus of his laboratory. The proteins encoded by this gene family are members of the helix-loop-helix class of transcription factors, whose mammalian homologues are proto-oncogenes.

The major aim of *Dr. Chaganti's* laboratory is to define the role played by genetic factors in the initiation and progression of malignant phenotypes and regulation of differentiation in transformed stem cells.

Dr. Chao's research interests focus on gene expression and regulation in mammalian cells. Molecular genetic techniques are applied in studying the gene encoding the nerve growth factor receptor and to analyze the role of the receptor in the mechanism of signal transduction by NGF and in the development of the nervous system.

A variety of research areas with relevance to human *in vitro* fertilization is the focus of *Dr. Cohen's* laboratory. These include the development of improved micromanipulations, which aid sperm in crossing the zona pellucida at will, and approaches in correcting polyspermic embryos. Embryo co-culture and pre-implantation genetic diagnosis are also topics of interest.

Dr. Fischman's research focuses on the cell and molecular biology of skeletal and cardiac muscle development. The identification of genes encoding novel muscle components, retroviral analyses of cell lineages, and targeted gene insertions are being employed to better define the steps involved in sarcomere assembly.

Dr. Freedman's laboratory is attempting to elucidate the molecular mechanisms by which DNA-binding proteins affect differential gene expression. His work is centered on the study of transcription factors that are inducible by steroids and other ligands, known collectively as the nuclear hormone receptor superfamily, and their direct role in mediating the regulatory events that control development and differentiation.

Several clinically relevant aspects of human genetics are under study in *Dr. German's* laboratory. The primary defect in Bloom's syndrome is being mapped with the eventual goal of cloning the gene involved. This syndrome illustrates the developmental consequences of somatic mutation. The molecular dissection of the pseudoautosomal and adjoining regions of human sex chromosomes is also an area of interest.

One focus of research in *Dr. Gershengorn's* laboratory is to delineate the structure-function relationships of guanine nucleotide (G)-binding protein-coupled receptors using receptor mutants and chimeras. Two receptors that are activated by peptides—thyrotropin-releasing hormone (TRH) and calcitonin—are under investigation. Another focus of research is the use of adenovirus-mediated gene transfer for basic studies of receptor biology and for gene therapy.

Dr. Gumbiner's group is investigating the functions of cell adhesion molecules and intercellular junctions in tissue morphogenesis. The main emphases are on the molecular mechanisms of cadherin function (including the roles of associated cytoplasmic proteins), and their roles in the early development of the frog *Xenopus laevis.*

Research in *Dr. Hajjar's* lab focuses on the role viruses may play in activating coagulation proteases with adhesion proteins on the blood vessel wall and the atherosclerotic process.

The role of molecular chaperones in catalyzing the folding of newly synthesized polypeptides is the major focus of *Dr. Hartl's* research. How members of the *hsp70* and *hsp60* families direct protein folding and intracellular sorting is of particular interest.

Dr. Jaffe is studying stimulus-response coupling and signal transduction in endothelial cells. Current research includes identification of the seven membrane-spanning domain receptor family expressed by endothelial cells, and characterization of signal transduction pathways activated by thrombin in endothelial cells.

The focus of *Dr. Jasin's* work is to develop methods to precisely modify the genome of mammalian cells. Also of interest is the repair of DNA double-stranded breaks in the genome of mammalian cells and germ-line and meiotic genome dynamics.

Dr. Klein is studying the effects of cardiac contractility and thyroid hormone on the regulation of cardiac myosin synthesis.

The roles of gene expression in cell differentiation and mammalian development are the two major interests of *Dr. Lai.* The approaches taken in the laboratory include the identification and analysis of a novel family of transcription factors that controls cell-specific gene expression.

Dr. Marks and *Dr. Rifkind* study the cellular and molecular mechanisms controlling coordinated gene expression and proliferation during induced cell differentiation. The principal experimental model is the murine erythroleukemia cell (MELC), a virally transformed red blood cell precursor arrested at a stage called the colony-forming cell in erythropoiesis. A number of defined chemical agents can induce MELCs to express the genetic program of erythroid differentiation. Present studies address the signal mechanisms triggered by inducing agents, the mechanism of induced gene expression, and the identification and cloning of genes implicated in the programmed cessation of cell proliferation.

Dr. Massague's research interests concern the mediation of intercellular communication by growth and differentiation factors. Much of his research is centered on understanding the activities of transformation growth factors (TGFs).

The research in *Dr. Mikawa's* laboratory is focused on the molecular mechanisms involved in cardiac differentiation and morphogenesis. The major experimental approach involves using recombinant retroviruses to modulate *in vivo* expression of genes encoding growth factors, cell adhesion proteins, and trans-acting DNA-binding proteins.

Dr. Moore's research concerns the mechanism of action of hematopoietic growth factors and interleukins in regulating the proliferation and differentiation of normal and leukemic hematopoietic stem cells. The regulation of factor production and modulation of receptors on various cell populations are analyzed. *In vivo* tumor models are being investigated to test the potential for cytokine treatment in intensified chemotherapy.

The focus of *Dr. Nachman's* laboratory is the endothelial cell membrane and the macromolecular assembly of fibrinolytic constituents that influence vascular non-thrombogenicity.

Dr. Nathan's efforts are aimed at understanding how phagocytic leukocytes kill microbes, tumor cells, and normal host elements at inflammatory sites. Investigations into the biochemical bases of cytotoxicity by macrophages and granulocytes are integrated into a context of cell biology and clinical investigation.

Dr. Pardee's research is concerned with the regulation of the actin cytoskeleton by actin-binding proteins. Regulatory proteins such as myosin, severin, and an actin-filament bundling factor have been isolated and are being analyzed for their roles in cell migration and neoplastic transformation.

The interaction of tyrosine kinase onco-proteins with membranes is the major interest of *Dr. Resh.* The focus is understanding how fatty acid modification of proteins influences subcellular targeting and signal transduction. The laboratory is defining the molecular basis for membrane attachment of fatty acylated proteins, as well as the enzymology of protein myristylation and palmitylation.

Dr. Robertson's research involves structural and functional analysis of biologically important RNA molecules. A current focus of interest is the RNA genome of the viroid-like hepatitis delta agent, recently shown to be a ribozyme by his laboratory.

The focus of *Dr. Rodriguez-Boulan's* laboratory is the regulation of normal and epithelial cell phenotypes. The roles of protein targeting, cytoskeleton regulatory signals, and growth factors are studied using biochemical, immunological, virological, and molecular techniques in combination with modern structural and electron microscopic procedures.

Dr. Rosen's research is concerned with the role of activated *src*-related tyrosine protein kinases and the IGF-I receptor in human carcinoma of the colon and breast. Current projects include analyses of *src* and *lck* activation in colo-rectal cancer and how the mitogenic signal induced by IGFs in breast cancer is transduced.

The work in *Dr. Rothman's* laboratory is focused on intracellular protein sorting. An *in vitro* transport system derived from Golgi stacks has been developed, allowing biochemical analysis of protein sorting and the mechanisms of vesicle budding and fusion.

Dr. Silverstein's interests concern the molecular pathogenesis of thrombosis and atherosclerosis. His laboratory is pursuing the mechanisms of cell signaling through adhesion receptors, their structure and function.

Dr. Sonenberg's long-range objective is a molecular description of membrane transduction of peptide hormonal messages after interaction with a specific membrane receptor or other membrane component.

Dr. Staiano-Coico's research focuses on the mesenchymal-epithelial interaction that occurs during wound repair and tissue regeneration. Molecular, biochemical, and flow cytometric techniques are used to examine the mechanisms of growth and differentiation regulation within the skin.

The main focus of *Dr. Traktman's* research is molecular genetic and biochemical analysis of the *Vaccinia* virus. Of particular interest are temporal regulation of gene expression, coordination of viral DNA replication, and the role(s) of the virally encoded protein kinases and phosphatase.

Dr. Wagner's laboratory is interested in the effects of Nerve Growth Factor, Fibroblast Growth Factor, and other signaling molecules on the development, survival, and differentiation of neural cells. In particular he is interested in the signal transduction pathways that are under the control of these molecules, and the ways they regulate gene expression, morphological differentiation, and enzymatic activity. He is also interested in the role of these molecules in the response to traumatic injury, ischemia, neurodegenerative diseases, and aging.

Dr. Wiedmann's research is focused on the translocation of proteins across membranes. Identification and analysis of proteins that participate in moving nascent polypeptides across the endoplasmic reticular membrane is of particular interest.

The main interest of *Dr. Zakim's* laboratory is solvent-solute interactions in membranes. Polymethylene chains are the solvent and proteins of small apolar molecules are solutes. Major emphasis is given to how these nonspecific effects regulate the functions of integral membrane proteins.

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Program in Immunology

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Research Activities

The main interests of the Immunology faculty are focused on the complex molecular and cellular mechanisms responsible for the development and regulation of the immune system. Research programs can be grouped into three main areas: (1) immunogenetics of cell surface molecules involved in the differentiation and function of normal and malignant lymphoid cells; (2) cellular immunology of the interactions between cells and their secreted products, and (3) tumor immunology of the transformed tumor cell and its host, aimed at designing possible diagnostic and therapeutic strategies. Research in all three areas involves studies using both animal models and human cells. Immunology is multidisciplinary in its approaches and has generated its own methodology (such as the production of monoclonal antibodies, and the continuous *in vitro* growth and cloning of lymphoid cells), in addition to using the methods of other disciplines, including biochemistry and molecular biology. For example, the analysis of the biological significance of a given lymphoid cell surface antigen is not only studied using classical genetics and in functional assays using monoclonal antibodies, but also by isolating the molecule and defining its structure using biochemical techniques and characterizing its gene with the tools of molecular biology. Thus, the general approach of the research program is to define immunological events at the biological, biochemical and molecular levels.

In the field of tumor immunology, *Dr. Albino's* laboratory is examining the role of specific oncogenes in the pathogenesis of malignant melanoma and renal carcinoma. This includes a comprehensive study of the steps required for the transformation of human melanocytes and proxymal tubule cells. In addition, this laboratory also studies the structure and function of melanoma cell-surface differentiation proteins and their gene sequences.

Dr. Chiorazzi's laboratory is investigating the mechanisms and cellular interactions involved in B lymphocyte activation and differentiation to antibody secreting cells. Studies of selected lymphoid cell surface receptors and their ligands are integral components of these analyses. Monoclonal populations of lymphoid cells, derived by

either Epstein-Barr virus transformation or somatic cell hybridization, are frequently employed in this approach. Structural and functional studies of antibodies produced in certain autoimmune disorders have provided basic clues to the relationship between normal and disease states. Autoimmune and allergic disorders as well as the chronic lymphoid malignancies are this laboratory's clinical interests.

Dr. Crow is a member of the Cellular Immunology Laboratory at the Hospital for Special Surgery. Two of the collaborative projects she is involved in are: the role of microbial superantigens in T-cell activation, B cell differentiation, and autoimmune diseases; and the investigation of autoantigen-reactive T cells in patients with systemic lupus erythematosus.

The central themes for *Dr. Dupont's* laboratory are the characterization of the genetic composition of the genes of the human major histocompatibility complex (MHC); the investigation of the molecular genetic basis for the expression of these extensive genetic polymorphisms of the MHC-encoded cell surface antigens as detected in the population; and the biological role of MHC gene products in immunoregulation and other biological functions. The laboratory is also involved in investigations in the area of transplantation immunology, particularly in relation to the understanding of mechanisms responsible for graft vs. host disease.

The major focus of the laboratory of *Dr. Elkon* is the investigation of mechanisms of autoimmunity. His current areas of study include: the role of antigen in T-cell activation, molecular defects in lupus T cells, analysis of growth and differentiation of MRL/lpr lymphocyte progenitor and adoptive transfer of lupus cell subsets into SCID mice.

Dr. Friedman is a member of the Cellular Immunology Laboratory at the Hospital for Special Surgery. Two of the collaborative projects he is involved in are: the investigation of the mechanisms involved in T helper cell-dependent B cell activation; and the helper T cell-dependent generation of cytolytic T lymphocyte activity.

For the mouse, the majority of genes encoding lymphocyte antigens are organized in distinct multigene families positioned on several chromosomes. Study of these gene clusters continues to be the major theme of *Dr. Hämmerling's* efforts. The immunogenetics of murine and human lymphoid and hemopoietic cell surface antigens using monoclonal antibodies is another area of Dr. Hämmerling's studies, with special emphasis on their role in T cell activation.

Dr. Houghton's research program is investigating the expression and regulation of antigens by human tumor cells. Genes coding for these antigens are being identified, sequenced and expressed. The role of differentiation and malignant transformation in the expression of these antigens is an area of active study. Antigens on tumor cells that are potential targets for recognition by the immune system are of particular interest.

Dr. Ivashkiv's research focuses on understanding monocyte and T lymphocyte gene regulation at sites of inflammation and in autoimmune disease. Two major areas of interest are: (1) monocyte gene activation in inflammatory arthritis, and (2) cytokine and HLA Class II gene regulation in autoimmune disease.

The primary investigative interests of *Dr. Kimberly's* laboratory are the study of human Fcγ receptor polymorphisms, the functional capacity of different polymorphic forms and their relationship to the pathogenesis of autoimmune disease. Studies are being conducted in the following areas: Molecular variants of FcγRI; signal transduction of FcγR isoforms; allelic polymorphisms and receptor function; and glycoforms and receptor function.

The molecular genetics of the human major histocompatibility complex or HLA genes is the major area of study of *Dr. Lee's* laboratory. Her goals are to identify and characterize genes and their products that govern the tissue specific expression of class

II genes. These studies involve the analysis of defects in expression of mutant cell lines derived from immunodeficiency patients. In addition, the laboratory is investigating regulatory polymorphisms associated with different alleles.

Investigations of the glycoproteins and glycolipids of human tumor cells and normal cells are the focus of research in *Dr. Lloyd's* laboratory. Particular emphasis has been placed on the biochemical identification and characterization of these components.

Dr. Murray has several inter-related research interests. These include (1) macrophage activation for antimicrobial activity, (2) intracellular infections caused by *Toxoplasma gondii* and *Leishmania donovani*, (3) interferon-gamma, and (4) the AIDS T cell defect.

Dr. Nathan's efforts are aimed at understanding how phagocytic leukocytes kill microbes, tumor cells, and normal host elements at inflammatory sites. Investigations into the biochemical bases of cytotoxicity by macrophages and granulocytes are integrated into a context of cell biology and clinical investigation.

The focus of *Dr. Nikolic-Zugic's* laboratory is on the ontogeny of T cells and their differentiation in the thymus. This laboratory is also investigating the interaction of the major histocompatibility complex (MHC) encoded molecules and the TCR during the positive selection of T cells in the thymus.

Dr. Old's research is concerned with the development of two new approaches to cancer therapy: tumor necrosis factor (TNF) and monoclonal antibodies directed against surface determinants on malignant cells. The latter is part of a general effort to analyze the cell surface of human and murine tumors, with the aim to characterize the important surface molecules, mostly with monoclonal antibodies and other serological procedures.

The principal objective of *Dr. O'Reilly's* Bone Marrow Transplantation Program is the development and improvement of transplantation approaches for the treatment of lethal disorders of the blood system through an integrated program of clinical and basic research in immunology, hematology, genetics, and transplantation biology.

The focus of the research performed in *Dr. Petrie's* laboratory is on the events which actively or indirectly shape the antigen-specific repertoire of developing T lymphocytes. The genetic mechanisms regulating the function of in-frame rearrangements, MHC interaction, and survival among developing T cells, and their roles in the production and selection of T lymphocytes, are now under investigation.

Dr. Posnett's laboratory is interested in basic problems of immunology. The approach is primarily molecular. The topics under study include the human T cell antigen receptor and several lymphocyte membrane molecules that may serve as lymphokine receptors. In the former case he is interested in understanding the process of antigen/MHC recognition by T cells. Studies are focusing on T cell antigen receptor V gene usage and its relationship with antigen/MHC reactivity. Also of interest are disease associations with the T cell antigen receptor genes. He is also cloning the genes of several putative lymphokine receptors. These studies are aimed at understanding the function of these membrane activation antigens.

Dr. Russo's research is concerned with the role of MHC molecules in regulation of the immune response. Two major areas are under investigation: (1) the dual function of MHC class II molecules in the induction of self-tolerance and in the biology of the autoreactive T-cell network, (2) the relationship between selective loss of MHC class I molecules by tumor cells and tumor progression.

The main interest of the laboratory of *Dr. Salmon* is to examine the structure-function relationships among Fcγ receptors (FcγR) on human phagocytes and their implication for susceptibility to and pathogenesis of systemic lupus erythematosus. Studies are being conducted in structure-function relationships among the alleles of FcγRIII and FcγII; mechanism for the altered phagocytosis among HLA-DR2 and

DR3-positive disease-free subjects and SLE patients; and characterization of the nature of association of HLA class II antigens and the defect in FcγR-mediated function.

Dr. Schwab's research focuses on age-associated changes in the activation signal transduction mechanism via the T-cell receptor CD3 complex and IL-2 receptor.

Two of *Dr. Smith's* ongoing projects are: focusing on the IL-2-stimulated molecular pathways that promote cell cycle progression; and the other is directed towards understanding the cellular and molecular basis for IL-2-promoted differentiation of naive T cells to memory T cells.

The system being studied in *Dr. Stoeckle's* laboratory is the regulation of pro-inflammatory cytokine genes in fibroblasts in response to interleukin-1 (IL-1).

Dr. Stutman's research is focused in two areas: (1) the ontogeny, maintenance and involution of functional T cells, including T cell subsets and the role of the thymus proper in such processes, and (2) the immunological components of the tumor-host interaction, especially the production of cytotoxic effector cells which can kill tumor cells by production of tumor necrosis factor (TNF) and other lytic molecules.

Dr. Weksler's research concerns two areas: (1) the biology of autoreactive T lymphocytes and (2) the immunobiology of aging. The former studies are aimed at understanding the development and regulation of the immune system; the latter at understanding the biological processes that lead to the diseases of aging.

Dr. Yang's laboratory is conducting studies of the molecular mechanisms controlling class I MHC gene expression during cellular differentiation and neoplastic transformation, as well as the biological role of class I MHC determinants in tissue transplantation. Another area of study is the activation and differentiation of T lymphocytes and characterization of T-lymphocyte differentiation antigens and their function.

Recent Publications

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Program in Molecular Biology

Faculty

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Kenneth I. Berns
Peter Besmer
Anthony M. C. Brown
Moses V. Chao
Robert DeLotto
Dale Dorsett
Erik Falck-Pedersen
Lorraine J. Gudas
Neil R. Hackett
William K. Holloman
Jerard Hurwitz
Andrew Koff
Elizabeth Lacy
Monika Lusky
Arthur J. Lustig
Kenneth J. Marians
Michael O'Donnell
Lee Ann Niswander
Mary Ann Osley
Jeffrey V. Ravetch
Michael B. Sheffery
Stewart Shuman
Paul Tempst
Paula Traktman
Andrew Zelenetz

Research Activities

The faculty of the Graduate Program in Molecular Biology offers graduate research training in a variety of systems on problems related to the replication, transcription, translation and function of genetic information in developing organisms and differentiating cells.The research activities of the faculty can be divided into four broad areas of study: DNA replication and recombination; regulation of RNA synthesis and processing; receptors and their role in cell function and differentiation; and retroviruses, proto-oncogenes, and development.

DNA Replication and Recombination

DNA replication in prokaryotes is under study in the laboratories of *Dr. Marians* and *Dr. O'Donnell*. Dr. Marians focuses on studies of the enzymological mechanisms of DNA replication in *Escherichia coli,* using cell-free systems.The use of *in vitro* DNA replication systems composed of purified replication proteins enables detailed analyses of the interaction of the replication proteins with each other and with the DNA template.The role of topology in DNA replication, as well as the mechanisms of DNA topoisomerases, is also under study in his lab.A detailed examination of the molecular mechanics of DNA replication is also the focus of Dr. O'Donnell's laboratory.The dynamic motions on templates of the multi-protein replicative polymerase of *E.coli* and its interaction with other proteins at the replication fork are under study. Dr. O'Donnell is also investigating the control of replication initiation in Epstein-Barr virus.

Faculty investigating eukaryotic DNA replication employ several different viral systems. *Dr. Berns* uses the life cycle of the human adeno-associated virus AAV2 to model how gene expression and DNA replication are regulated. *Dr. Hurwitz*'s

laboratory uses the adeno and SV40 viral DNA replication systems as probes for the enzymatic mechanisms of cellular DNA replication. The regulation of bovine papilloma virus DNA replication is studied by *Dr. Lusky* using molecular genetics to define and characterize the viral genes required for replication *in vivo* and using biochemical approaches to study BPV DNA replication *in vitro*. The replication of AAV, adenovirus, SV40, and BPV require host cellular proteins; thus these viral systems also allow these investigators to study the endogenous mechanisms for DNA replication in mammalian cells.

Dr. Traktman's laboratory studies the replication of vaccinia virus, a large DNA virus that encodes its own DNA replication machinery. Both biochemical and molecular genetic techniques are employed to define the genes of vaccinia virus that are required for its replication.

Dr. Koff's laboratory is studying the biochemical mechanisms that regulate the eukaryotic cell cycle. His research focuses on a CDK inhibitor $p27^{KIP1}$ and its role in S phase entry and development.

The molecular processes controlling the structure, function, and genetic properties of chromosomes are being studied by the laboratories of *Drs. Lustig* and *Hackett*. Using molecular genetics and biochemistry, Dr. Lustig is investigating the mechanisms that have evolved for replicating telomeres, the unique ends of chromosomes required for stability, and the role these sequences play in chromosome segregation and recombination. Dr. Hackett is also interested in the structure of the bacterial genome and how it changes over time. His immediate objective is to construct detailed restriction maps of the genomes of several related isolates of *Halobacterium halobium*. Comparisons will reveal how genome structure evolves both normally and in response to selective pressure.

Another key cellular process that occurs on DNA is the exchange of genetic information through the process of recombination. *Dr. Holloman*'s laboratory studies the genes and the enzymes involved in this complicated process. Model studies focus on the mechanism of synapsis and DNA strand exchange.

Regulation of RNA Synthesis and Processing

Many aspects of the regulation of gene transcription and RNA processing are under active investigation by members of the Molecular Biology Program. These include the definition of controlling DNA and RNA sequences, the identification and characterization of the proteins and enzymes involved, and the elucidation of the mechanisms that dictate temporal and spatial patterns of gene expression.

Using genetic and molecular biological techniques, *Dr. Osley* is investigating the basis of the periodic expression of the histone genes in yeast and the connection between chromatin structure and gene transcription.

Research in *Dr. Sheffery*'s laboratory is directed at understanding how proteins and DNA interact to form structures that influence gene transcription, using the mouse globin genes as a model. Particular effort is devoted to understanding tissue-specific gene expression.

In a related effort, the basis of sequence-specific recognition of DNA by proteins is studied by *Dr. Barany* using a combination of molecular biology and biochemistry. One of these proteins, *Taq* ligase, is also used for detecting genetic diseases.

Dr. Falck-Pedersen is characterizing the regulatory elements involved in eukaryotic transcription termination and RNA processing using genetically reconstructed adenovirus as a model vector. Both biochemical and genetic aspects of transcriptional control, with particular emphasis on transcription termination in purified *in vitro* systems, are under study by *Dr. Shuman* using vaccinia virus as a model.

Dr. Dorsett's laboratory is using both genetic and molecular biological techniques to define the *cis*- and *trans*-acting factors that regulate virus-like transposons in *Drosophila*. These transposons are responsible for a number of naturally occurring mutations in *Drosophila* and have been shown to affect the expression of the mutated host genes at the level of transcription.

Dr. Hurwitz's group studies the enzymes and enzymological processes involved in mRNA splicing in human cells.

Receptors and Their Role in Cell Function and Differentiation

Several laboratories are investigating receptors that transmit signals to the interior of the cell after forming a complex with a specific ligand.

In a series of experiments in *Dr. Ravetch*'s laboratory, the molecular genetic analysis of cell surface receptor proteins is being conducted. Receptor modulation, mechanism of signal transduction, and developmental regulation are being studied by isolation and characterization of genes that code for proteins binding immunoglogulins (FC receptors), by studying the interaction of the malaria producing parasite with the erythrocyte, and by characterizing the activated macrophage phenotype.

Dr. Chao's laboratory is studying the mechanism of action of growth factor receptors, such as those interacting with NGF, FGF, EGF, and TNF. In particular, the molecular features that distinguish NGF signaling through its receptor tyrosine kinase are being defined in order to link receptor-mediated events with the steps leading to neuronal differentiation and cell survival.

Using the generation of transgenic mice as the major experimental tool, *Dr. Lacy* is studying the regulation and function of the CD4 and CD8 cell-surface glycoproteins during T-cell maturation in the thymus. CD4 and CD8, respectively, recognize and bind to nonpolymorphic regions on class II and class I major histocompatability complex (MHC) proteins; their interactions with the MHC proteins contribute to the signals transduced by the T-cell receptor during T-cell development and activation.

Retroviruses, Proto-oncogenes, and Development

The research activities of the Molecular Biology faculty in this area are quite diverse and include studies on induced neoplastic diseases, the role of proto-oncogenes in cell and tissue differentiation, embryonic axis formation in *Drosophila*, and gene function in the early mouse embryo.

The major objective of *Dr. Zelentz's* laboratory is the elucidation of the molecular basis of the induction of neoplastic disease. Research focuses on the molecular events involved in the genesis and progression of hematolymphoid malignancies. Of particular interest are the mechanisms underlying chromosomal translocation in cancer.

The current research goal in *Dr. Besmer*'s laboratory is to understand the function of the proto-oncogene c-*kit*, a transmembrane receptor kinase. The c-*kit* ligand has

been cloned and molecular aspects of c-*kit* mediated signal transmission are being investigated in hematopoietic cell differentiation and development.

Dr. Brown's laboratory is studying a family of genes (*Wnt* genes) that encode intercellular signaling molecules active in embryogenesis and tumorigenesis. A major focus is the protein product of the proto-oncogene *Wnt*-1 and its mechanism of action in cell culture systems.

Dr. Tempst's laboratory studies the regulation, processing and activities of antibacterial peptides, which are major components of the insect immune system. High resolution 2D gel electrophoresis and high sensitivity sequencing techniques are being developed to investigate cellular events at the single protein level.

Dr. DeLotto uses *Drosophila* as an experimental organism to study the mechanisms underlying the formation of the dorsal-ventral axis during embryonic development. Several of the components of the d-v system, *snake*, *easter*, and *gastrulation defective*, are extracellular serine proteases which play a role in a signal transduction cascade. The laboratory is investigating the biochemical interactions of these proteins *in vitro* and *in vivo*.

Dr. Niswander's laboratory is studying the molecular and cellular mechanisms by which embryonic growth is regulated and positional information is specified. Her research focuses on the developing vertebrate limb and the role of FGF-4 and other signaling molecules in pattern formation.

Dr. Lacy's and *Dr. Gudas'* laboratories investigate cell differentiation during mammalian development. Dr. Lacy's group is working on identifying and isolating genes that are required during early post-implantation mouse development by generating insertional mutations in the germ line of transgenic mice. The Gudas laboratory has chosen to employ cultured murine embryonic teratocarcinoma stem cell lines as a model system for molecular studies of embryonic cell differentiation. Of particular interest are the mechanisms by which retinoic acid differentially controls gene expression during the differentiation process and the loss of tumorigenicity of the stem cells.

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Program in Neuroscience

Faculty

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Dana H. Bovbjerg
Michael Caudy
Moses Chao
Arthur J. L. Cooper
Robert Duvoisin
Donald Fischman
Henry M. Furneaux
Sam Gandy
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Bernice Grafstein
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Barbara Hempstead
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Jerome B. Posner
Donald J. Reis
David A. Ruggiero
Gerard P. Smith
Peter E. Stokes
Miklos Toth
Jonathan D. Victor
Bruce T. Volpe
John A. Wagner

Research Activities

Members of the program in Neuroscience use a wide variety of scientific disciplines to study the development and function of the nervous system, including molecular genetics, biochemistry, pharmacology, neuroanatomy, electrophysiology, molecular biology, and behavior. They work at the molecular, cellular, and organismal levels in many animals including rodents, birds, *Drosophila,* reptiles, and *aplysia,* as well as in humans. The research interests of the program cover the entire range of neuroscience, including the regulation of neural development, neuronal plasticity, control of neurotransmitter synthesis and release, learning, the response of neurons and neural tissue to injury, the regulation of gene expression, endocrine function, vision and other sensory systems, information processing, and behavior. Many members of the program have a special interest in questions that are particularly relevant to human disease, and their research has important implications for topics such as the regulation of pain, neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, neural tumors, stroke, addiction, and aging.

Dr. Baker studies the factors underlying the determination and maintenance of neuronal phenotype. Using the olfactory system as a model, Dr. Baker focuses her research on neurotransmitter expression during development and aging as well as in response to deafferenting lesions. Immunocytochemical, neurochemical, *in situ* hybridization, molecular biological, and neuronal tracing techniques are utilized in these studies.

Dr. Blasberg's major research interests include the physiology and metabolism of brain tumors and the *in vivo* study of neuroreceptor systems using positron emission

tomography (PET). He has set up a laboratory for performing quantitative autoradiography and biodistribution studies in small animals to complement the PET program. Active areas of research that are being pursued focus on: a) developing quantitative imaging techniques for measuring the rate of tumor cell proliferation, b) studying the potential of viral therapy for brain tumors, and c) investigating new immunoreactive agents that target unique, tumor-specific epitopes in gliomas. These tumor-specific reagents will be used for new diagnostic and targeted radioimmunotherapy.

Dr. Bovbjerg's major research interest is the interactions between the brain and the immune system in both humans and animal models. He is particularly interested in classically conditioned changes in immune function. Research techniques include a variety of *in vitro* and *in vivo* assessments of immune function, as well as a variety of psychobehavioral methodologies. Additional research interests include: the effects of naturalistic and experimental "stress" on immune function in humans; classical conditioning processes in humans; and behavioral effects of immunologic manipulation.

Dr. Caudy is interested in the molecular genetic mechanisms which control neuronal pattern formation during development. He is studying a network of cell determination genes which control the switch between neuronal and non-neuronal cell fates in *Drosophila* embryos. These genes encode a family of DNA-binding transcription factors ("helix-loop-helix" proteins) whose human homologues are proto-oncogenes.

Dr. Chao's laboratory is interested in linking the signal transduction events in the central nervous system with specific transcriptional processes that promote cell differentiation. They have been studying the mechanism of action of NGF, a neurotrophic factor responsible for cell survival and differentiation. They are pursuing the definition of the NGF receptor complex, including the targets of tyrosine kinase phosphorylation, and correlating structural features of the receptor with function using molecular and biochemical approaches and transgenic animals.

Dr. Cooper's research interests include α-Keto acid chemistry and biochemistry; pyridoxal 5'-phosphate enzymes; investigations of enzyme mechanisms; design of enzyme inhibitors as drugs; amino acid and ammonia metabolism in normal and disease states; cerebral energy metabolism (with particular emphasis on the malate-aspartate shuttle) and its disruption in various disease states; design and use of molecules labeled with short-lived radioisotopes for positron emission tomography of the human tissues and for tracer studies in animals; neurochemical consequences of cerebral ischemia; molecular biology of glutamine transaminase K/cysteine *S*-conjugate β-lyase, ω-amidase in rat kidney; and mitochondrial defects in Alzheimer's disease.

Dr. Duvoisin's laboratory is studying the molecular basis of retinal function. Molecular cloning has revealed a greater than expected complexity of neurotransmitter receptors and ion channels. The retina, with its well-studied circuitry, is being used to analyze the relationship between molecular diversity and information processing. Ongoing research focuses on glutamate receptors and their role in generating the ON and OFF pathways.

Dr. Fischman is examining gene action within developing muscle cells of the avian embryo. Using retroviral vectors, he is defining the lineages of somitic cells which give rise to limb muscle and altering the expression of selected genes required for normal myogenesis and muscle regeneration.

Dr. Furneaux's laboratory studies a unique group of tumor antigens which are normally exclusively expressed in neurons. A number of these antigens have been cloned and characterized, such as HuD, which is a neuronal-specific RNA binding protein and is highly homologous to a *Drosophila* protein (Elav) which controls

neuronal cell fate. Recently we have cloned the target antigen in Lambert Eaton syndrome and have shown that it is the B subunit of the Ca channel complex.

Dr. Gandy's research focuses on Alzheimer's disease, the most common cause of senile dementia. Cerebral deposition of β/A4-amyloid protein is a key feature of the neuropathology of the disease. β/A4-amyloid is derived by proteolysis from a transmembrane precursor, the β/A4-amyloid precursor protein (APP), and mutations in APP segregate with clinical phenotypes of familial Alzheimer's disease. APP is a phosphoprotein, and protein phosphorylation plays a key role in regulating the activity of a standard APP proteolytic pathway which prevents amyloid deposition ("non-amyloidogenic"). Identifying the regulatory components of the APP processing apparatus is the major goal of Dr. Gandy's laboratory.

Dr. Gardner studies how neurons use chemical synaptic transmission to communicate with one another. Neurons in ganglia of the mollusk *aplysia* are probed by intracellular recording, voltage clamping, patch clamping, and computer-based analysis to yield principles of organization of cell networks. One project focuses on properties of transmitter-activated channels which are altered to produce different postsynaptic currents. A second project combines neurophysiology with artificial intelligence techniques to ask how neuronal biophysics coordinates the activity of neurons in a network.

Dr. Gibbs' research focuses on the neurobiology of motivated behaviors, especially the neuroendocrine mechanisms controlling feeding behavior in animals. The focus of current work is the role of brain-gut peptides in the regulation of short-term food intake.

Dr. Gibson focuses on the relation of signal transduction systems (e.g. calcium, PI cascade and cyclic AMP) to oxidative metabolism, neurotransmitters, altered brain function, cell death and gene expression. These interactions are researched in tissue culture and in animal models of conditions that alter memory and other mental functions in man (aging, hypoxia/ischemia and thiamine deficiency) as well as in tissues from Alzheimer patients.

Dr. Goldman is interested in cellular regeneration in the adult brain. His research is focused upon the molecular mechanisms subserving neural production, migration and differentiation in neurogenic regions of the adult brain. These cellular events are examined both *in vivo* and *in vitro,* with the aim of determining the regulatory constraints on neurogenesis and neuroblastic migration in the adult CNS.

Dr. Grafstein's primary research interest is in nerve regeneration. At present she is working to characterize the function of a prominent glycoprotein in goldfish brain that has been implicated in neuronal plasticity, including nerve regeneration and learning. Her studies have shown that the protein is primarily localized in non-neural cells, including the meninges, outer wall of blood vessels and leucocytes. Thus this protein may play a role in the interaction between the nervous system and the immune system. Among the techniques used in Dr. Grafstein's laboratory are isotope tracer studies, high resolution autoradiography, immunocytochemistry, electron microscopy and 2-dimensional gel electrophoresis.

Dr. Greenberg focuses on the neuroendocrine mechanisms that control feeding behavior. Specifically, she is investigating neural and hormonal mechanisms mediating satiety induced by ingested fats and the mechanisms underlying increased fat intake in normal and genetically obese animal models.

Dr. Hempstead's laboratory examines the effects of neurotrophic factors on the survival and differentiation of responsive neurons. Specifically, the lab investigates the

intracellular pathways utilized by NGF to convey a differentiative, as compared to a proliferative response to growth factor addition.The contributions of both transcriptional activation of genes required for differentiation, and the biochemical interactions of proteins activated by the NGF receptor tyrosine kinase are being investigated. Research techniques include molecular cloning of transcriptionally regulated genes, *in situ* analysis to determine the localization of novel gene transcripts, and cell transfection to modify the intracellular enzymes required for NGF signaling.

Dr. Hirsch's research program includes using the new techniques of functional magnetic resonance (MR) to understand the signal transmission and network schemes employed by the human brain to code visual and other sensory information. Questions of visual information processing are also addressed by the Vision Lab Group using psychophysical assessments of visual function in conjunction with medical imaging assessments of brain tumors or focal injury.

Dr. Inturrisi studies the molecular basis for the pharmacodynamic effects of opioids and the factors that regulate the endogenous opioid peptide system.The mechanisms responsible for the development of tolerance to morphine and related opioid analgesics are not well understood.The competitive NMDA (N-methyl-D-aspartate) receptor antagonist LY274614 can attentuate or reverse the development of tolerance to morphine's analgesic effects. Some of the biochemical changes that occur with tolerance are the result of alterations in gene expression.The ability of NMDA receptor antagonists to prevent morphine tolerance is being used as a strategy with which to localize the biochemical and molecular changes that occur in tolerance.These studies are examining the endogenous opioid peptides and the recently cloned opioid receptors.The techniques of neuroscience and molecular biology are employed including, cloning, Northern analysis and a new solution hybridization technique.

Dr. Joh's laboratory is studying molecular biology of the neurotransmitter enzyme genes.The studies include structure/function analysis of these genes, gene regulation at transcription level, transgenic mouse models of genetically altered neurotransmission, targeted gene expression using defective HSV-1 viral vectors and gene therapy for degenerative brain disorders.

Dr. MacLeish's research program focuses primarily on the functional organization of the vertebrate retina. Dissociated neurons from adult amphibian and primate retina are employed to study the electrical properties of identified cells and the physiological properties of synapses formed among the retinal neurons *in vitro*. Voltage-sensitive dyes along with conventional intracellular recording techniques are used to measure electrical activity.A separate area of study is the trans-differentiation of retinal pigment epithelium into neural retina, a process that occurs in adult newts and salamanders. Antibody markers are being generated to describe the regeneration process in more molecular terms and a culture system is being refined to determine the role of soluble factors in regeneration.

Dr. Milner studies the cellular basis for transmitter interactions in the septo-hippocampal pathway important in learning and memory; between opioid neurons in the hippocampal formation which are involved in seizures; and reticulospinal neurons that are important in cardiovascular regulation. All three studies utilize either dual labeling immunocytochemistry techniques or immunocytochemical methods combined with tract tracing techniques at the electron microscopic level of analysis.The major transmitters of interest include catecholamines, acetylcholine, opioids and neuropeptide Y.

Dr. Nedergaard examines neuronal-glial signaling within the brain by combining intracellular calcium imaging with electrophysiological measurements. Current projects

include: 1) Astrocyte to neuron signaling *in vitro* and *in vivo.* 2) Gap junction mediated signaling within cultured brain cells. 3) Studies on spreading depression spontaneously evoked in brain ischemia and trauma. 4) pH regulatory mechanisms within neurons and astrocytes.

Dr. Okamoto studies the neuropharmacologic bases of the drug dependence produced by centrally acting drugs in adults and neonates exposed to drugs during their fetal period. Central nervous system depressant drugs, i.e. alcohol, barbiturates and benzodiazapines have been her major interest. Electrophysiologic, neurochemical and behavioral effects are studied during acute and chronic drug treatment: functional and cellular mechanisms for the tolerance and dependence production are investigated: chronic effects of these drugs are studied on developing synapses and on the maturation of the nervous system.

Dr. Pasternak studies the pharmacology of opioid receptors at the molecular, cellular, and systems level. The major focus is the identification and characterization both biochemically and pharmacologically of novel opioid receptor subtypes. In addition to traditional synthetic organic chemistry with structure-activity approaches, radioreceptor binding and second messenger studies, the laboratory has a major focus on molecular biology and has identified several new putative opioid receptor subtypes from PCR studies and is evaluating them. The functions of the clones for many of the various opioid receptor subtypes are being defined using antisense strategies both *in vitro* and *in vivo*. Additional work addresses the interactions of various brain regions in opioid function.

Dr. Pickel's laboratory carries out research to determine the cellular mechanisms for receptor mediated interactions between neurons containing catecholamines, opioids and other transmitters. This research principally uses electron microscopic immunocytochemistry, *in vivo* intracellular physiology, and *in situ* hybridization. The rat brain is the principal model system. The studies have implications for understanding normal and abnormal brain functions in human as related to rewarding and autonomic actions of opiates.

Dr. Plum, Chairman of the Department of Neurology and Neuroscience, focuses his research efforts on quantitative brain imaging studies of normal and abnormal cognitive mechanisms in humans. The goal is to improve understanding of the human conscious state.

Dr. Posner is interested in the characterization of "onconeural" antigens shared by the central nervous system and certain tumors. These antigens are identified by antibodies in the serum of patients with neurological disorders associated with non-neural tumors.

Dr. Reis' research interests are the central neural and neurochemical mechanisms governing control of the autonomic nervous system, cerebral blood flow, and metabolism. His research also includes mechanisms governing the death of brain neurons in response to aging and injury.

Dr. Ruggiero investigates neural networks within the central nervous system involved in the control of visceral reflex function during different phases of the sleep-wake cycle, responses to pain and exercise, and responses to stimuli that induce nausea. His laboratory is investigating functional polysynaptic pathways in forebrain involved in the affective, visceral and somatomotor concomitants of different forms of emotional expression and conscious behavior.

Dr. Smith focuses on the behavioral neuroscience of eating and its disorders. Current experiments include the measurement of central monoamines during eating

behavior, the role of gut peptides, such as cholecystokinin, to stop eating, and animal models of eating disorders using genetic and sham feeding rats.

Dr. Stokes is interested in neuroendocrine function in affective disease. Measurements of various brain endocrine axes function at various levels of these axes are obtained in patients with depression versus healthy normal controls and patients with other psychiatric diagnoses. Thyroid axis studies are aimed at characterizing the activity of the brain pituitary thyroid axis by static and dynamic tests during and depression and after recovery. Another area of interest is the investigation of lithium pharmacokinetics and pharmacology.

Dr. Toth's laboratory is interested in modeling diseases of the central nervous system in animals. The main approach is to generate knock-out and transgenic mice defective in certain gene functions and study the consequences of these alterations at the cellular, and molecular level. One direction is to study the serotonergic system and its involvement in disease. Disturbances in the serotonergic system occur in human disorders such as anxiety disorders and depressive syndromes. Another focus is to clone genes involved in epileptic seizure, and study how these genes and their dysfunction lead to neuronal hyperexcitability.

Dr. Victor studies visual processing at retinal and cortical levels. Research techniques include single-unit recording, evoked potentials, psychophysics, and mathematical modeling. Other research interests include novel approaches to nonlinear systems analysis and signal processing as applied to neural systems.

Dr. Volpe's laboratory studies learning and memory disorders that are common after ischemic and traumatic brain injury. The laboratory is also studying animal models of learning and memory dysfunction caused by ischemic injury, ablative injury, or toxic insult. Research techniques include the detailed characterization of the behavioral change, quantitative neuroanatomic studies, immunohistochemistry and *in situ* hybridization. The objective is to determine the extracellular factors governing cell viability and factors regulating tissue-specific gene expression after acute and chronic insults. Understanding the pathological processes involved in these models of brain injury could provide new insights into therapeutic interventions in certain chronic degeneration brain diseases.

Dr . Wagner's laboratory is interested in the effects of Nerve Growth Factor, Fibroblast Growth Factor, and other signaling molecules on the development, survival, and differentiation of neural cells. In particular he is interested in the signal transduction pathways that are under the control of these molecules, and the ways they regulate gene expression, morphological differentiation, and enzymatic activity. He is also interested in the role of these molecules in the response to traumatic injury, ischemia, neurodegenerative diseases, and aging.

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Program in Pharmacology

Faculty

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Research Activities

Dr. Bertino is interested in the transfer of drug resistant genes into hematopoietic cells: Viral vectors have been studied as methods of introducing drug resistant genes into mammalian cells in culture and into bone marrow cells. The aim is to produce long-term expression of drug resistant genes in hematopoietic stem cells. The purpose of these studies is to produce drug resistance of marrow stem cells, thus allowing larger doses of the desired drug to be utilized for therapy.

Mechanisms of natural and acquired resistance to folate antagonists and fluoropyrimidines: Human tumor cell lines and fresh human tumor samples (sarcoma, leukemia, colon cancer) are studied to determine mechanisms of resistance to these drugs. Sensitive assays to determine the molecular basis of drug resistance, including gene amplification, gene mutations, and transport and/or defects in drug catabolism have been developed.

Work has been initiated that has as its objective the relationship between oncogene expression and or lack of suppressor gene function on resistance to drugs. An inducible vector system has been developed to express transfected genes for this purpose.

Dr. Blanck's research interests include the characterization of the effects of anesthetics on intracellular calcium distribution in cardiac and neuronal cells. These studies are designed to further the understanding of how volatile anesthetics work to produce general anesthesia, their protective effects during ischemia, and their depressive effects on cardiac contractility. These varied effects appear to share a common mechanism of action, at least in part, that being the alteration of calcium ion availability and fluxes.

These changes are being studied by examining several calcium sensitive sites in cardiac and neuronal cells. Plasma membrane calcium channel density is characterized by measuring the number and affinity of drug binding sites in the presence of volatile

anesthetics. Studies are underway to characterize the functional properties of single calcium ion channels which have been incorporated into artificial lipid bilayer membranes.

Dr. Buck's interests focus on the structural and functional properties of small lipophilic intracellular signal molecules. Recent findings in several laboratories have demonstrated the potential of this class of molecules to serve as ligands for nuclear receptors. Well-studied examples are steroids and retinoic acids that have an important function in transcriptional regulation via the steroid receptor superfamily.

In recent years Dr. Buck has characterized two new intracellular messenger molecules, 14-hydroxy-*retro*-retinol (14-HRR) and anhydroretinol (AR). Lymphocyte activation and proliferation is critically dependent on an external source of vitamin A (retinol). After activation, lymphocytes produce 14-HRR from retinol. If 14-HRR production is blocked by AR, a physiologically occurring competitive 14-HRR antagonist, resting T cells cannot be activated and cycling cells die within hours.

The laboratory is trying to characterize in more detail the regulation and the biochemical pathway of 14-HRR/AR production and metabolism. Of utmost importance is the purification and cloning of the enzymes producing 14-HRR/AR and of intracellular 14-HRR binding proteins/receptors.

Dr. Chan is interested in the functions and interactions of prostaglandins and neurohypophysial peptides in the kidney and the uterus. Current research covers investigative studies from subcellular levels to the whole organism. Certain analogs of oxytocin and vasopressin have been found to stimulate urinary sodium and water excretion. This renal effect of the peptide appears to be mediated by renal prostaglandin release. The biochemical mechanisms of this peptide-induced prostaglandin release are the principal concerns of this research. Also studied are the renal activities of peptide analogs specifically synthesized for the project with the aim to discover specific prostaglandin-releasing and/or anti-vasopressin (anti-ADH) peptides that may be useful for the treatment of renal hypertension.

In the uterus, the roles of prostaglandins and oxytocin in the regulation of uterine contractions and termination of pregnancy are being investigated. This research seeks an understanding of the mechanism of initiation of labor, especially relating to preterm labor. Oxytocin-receptor and gap-junction formations in myometrial cells are important biochemical and morphological markers in the initiation of labor. Accordingly, effects of prostaglandins and oxytocin on the density of oxytocin-receptors and on the formation of gap-junctions in myometrial cells are studied. Highly potent oxytocin antagonists have been synthesized for this project and their application in the prevention of preterm labor in the pregnant rat model will be investigated. Also studied are the physiological roles of ovarian oxytocin and uterine prostaglandins in the function of the corpus luteum, as well as the potential of intervention of this ovarian-utero axis in the regulation of fertility or as causal factor in abortion.

Dr. Chou's research activity includes three areas: 1) developmental therapeutics of new antitumor and antiviral agents using synthetic compounds and plant products; 2) biochemical studies on selected compounds at molecular level with the aims of elucidating mechanism of action, selectivity of effect, or the development of drug resistance and cross-resistance, and 3) theoretical biology of deriving generalized equations based on the principle of mass-action law for dose-effect analysis, receptor topological analysis, and the quantitation of multiple drug interactions in terms of synergism and antagonism. In the first area, preclinical pharmacological studies have been conducted on acridone alkaloids such as glyfoline, and synthetic acridones as

anticancer agents, and on 2', 3'-dideonycytidine (DDC) as an anti-AIDS agent. In the second area, DNA intercalators, such as chrysophanol and acridine derivatives have been studied, as inhibitors of DNA topoisomerase type II. Topoisomerase II mediated-drug induced DNA cleavages and the inhibition of topoisomerase were examined by measuring the relaxation of supercoiled DNA, decatenation of kinetoplast DNA, and the stabilization of the cleavable complex. Monofunctional and/or bifunctional chloroethyl alkylating groups have been added to some of these molecules for active site and binding site studies. In the third area, the median-effect equation and the multiple drug-effect equation for isobologram and FA-CI plots have been derived and computer software for IBM-pc have been developed for automated data analysis. The method has been applied in various drug combination studies for anticancer agents, antiviral agents (anti-HIV, anti-HSV, etc.) and for immunosuppressants in organ transplantation.

Dr. Felsen's laboratory is interested in the role of inflammatory mediators or cytokines (including tumor necrosis factor, interleukins, PAF and arachidonic acid metabolites) in the genito-urinary tract. The role of these compounds both *in vitro* and *in vivo* is studied using a variety of techniques. In obstructive uropathy, renal function is assessed through measurement of renal blood flow, glomerular filtration rate, sodium, potassium, and water excretion and other parameters. *In vitro,* cell culture and molecular biological techniques are used to assess renal mediator synthesis by various elements of the genito-urinary tract. In interstitial cystitis (a chronic bladder disease), patient urine and tissue samples are examined for inflammatory mediators in an attempt to both better define this disease and to uncover new treatments for it. Additional studies in the prostate are involved with determining the role of newly described imidazoline receptors and inflammatory mediators in prostate growth and physiology.

Dr. Golde investigates the regulation of normal and neoplastic blood cell formation and the humoral mechanisms involved in modulating mature blood cell function. The biologic basis for the use of colony-stimulating factors (CSFs), interleukins, and certain cytokines is studied at the level of receptor interaction, intracellular signaling mechanisms, and transcriptional activation. The receptor for granulocyte-macrophage CSF (GM-CSF) is a focus of research with an emphasis on the function of soluble alpha subunits which arise by alternative splicing and a delineation of the early events in signal transduction. Cytokine regulation of transport through the glucose transporters is studied in model systems and in normal and neoplastic blood cells. The function of glucose transporters is also investigated in prostate cancer, breast cancer, and melanomas. Cytokines and CSFs are also studied with regard to activation of HIV proviral transcription in model systems using granulocytic, monocytic, and T-cell lines. Mature blood cell function is studied in terms of granulocyte, eosinophil, and monocyte-macrophage function in host defense, analyzing phagocytosis, microbial killing, antibody-mediated and antibody-independent cytotoxicity, and the transport of small molecules such as ascorbate.

The effect of growth hormone, insulin, and insulin-like growth factors is investigated with regard to their interaction with hematopoietic cells, particularly T lymphocytes. Unique virally transformed T-lymphocyte cell lines from patients with genetic abnormalities in responsiveness to insulin, growth hormone, and insulin growth factor-1 (IGF-1) are used in the laboratory to elucidate the cellular pharmacology of these hormones. Particular emphasis is placed on mechanisms of genetic and acquired insulin resistance.

Dr. Gross' research focuses on nitric oxide, a newly discovered biosignaling molecule whose functions are just beginning to be elucidated. Principal among the

known actions of nitric oxide is its key role in vascular homeostasis and blood pressure regulation, its mediation of cytotoxic and cytostatic effects of certain cells of the immune system, and its function as a chemical transmitter/second messenger in the brain. Deficient production of nitric oxide (also known as endothelium-derived relaxing factor; EDRF) by the vascular endothelium has been implicated in hypertension, atherosclerosis and diabetes. On the other hand, overproduction of nitric oxide may be responsible for the hypotension which occurs during bacterial sepsis and in response to the chemotherapeutic use of cytokines. The emphasis of Dr. Gross' research is to reveal biochemical mechanism(s) of nitric oxide synthesis, regulation and actions in physiology and disease.

The laboratory of *Dr. Gudas* has several long-term research aims. One major goal is to learn about the regulation of gene expression during mammalian cell differentiation, while another is to understand the mechanism by which vitamin A and its derivatives (retinoids) control both cellular differentiation and cellular proliferation. Retinoids exert effects on cell differentiation, pattern formation in development, limb regeneration, and the inhibition of the process of tumor formation. As a model differentiation system, the retinoic acid induced differentiation of murine teratocarcinoma stem cells is being studied. The teratocarcinoma stem cells differentiate into an epithelial cell type called parietal endoderm when they are treated with retinoic acid. A number of genes which are expressed at different times during this differentiation process have been cloned. Currently the structures of these genes are being determined, including the sequences of their promoters, in order to understand how their expression is regulated during differentiation. The actions of the nuclear receptors for retinoic acid, retinoic acid receptors α, β and γ, are being elucidated, as is the mechanism by which cyclic AMP can enhance the action of retinoids in this system. Finally, since the teratocarcinoma stem cells resemble pluripotent cells of the early mouse embryo, the expression of the teratocarcinoma differentiation related genes in transgenic mouse embryos and in early *Xenopus* embryos are being analyzed. These studies should lead to advances in the clinical uses of retinoids in cancer therapy and in dermatology.

Dr. Hemmings is interested in the synaptic mechanisms of general anesthetics, particularly the role of protein phosphorylation as a target for the effects of general anesthetics on synaptic transmission. Specific processes under study that are affected by general anesthetics and also regulated by protein phosphorylation include excitatory neurotransmitter release, excitatory neurotransmitter receptor function and inhibitory neurotransmitter receptor function. Experiments to probe the presynaptic effects of anesthetics employ a functional subcellular model of the synapse (synaptosomes), as well as purified components of the major presynaptic phosphorylation systems. The effects of various general anesthetics on depolarization- or secretagogue-induced neurotransmitter release and on changes in the phosphorylation of specific presynaptic proteins involved in the control of neurotransmitter release will be studied in synaptosomes. The effects of anesthetics on the activities of purified protein kinases, protein phosphatases, and on the phosphorylation and dephosphorylation of purified synaptic proteins by their appropriate purified protein kinases and protein phosphatases are also being studied. Experiments to probe the postsynaptic effects of anesthetics will employ purified neurotransmitter receptors.

A second line of research focuses on the characterization of neuronal protein phosphatases, mechanisms involved in the regulation of their activity, and their role in the regulation of neuronal function. This project involves the application of biochemical and immunological methods to the identification of neuronal phosphatases and their

regulators. The role of protein phosphatases in the control synaptic function will be examined using synaptosomes and cultured neuronal cells.

Dr. Inturrisi's research activities are directed toward the development of methods for the alleviation of pain. The genes that regulate the production of families of neuropeptides (called the endogenous opioid peptides or EOPs) have been identified and it is now possible to systematically investigate the factors that turn on and turn off opioid peptide gene expression. We have found that alterations in neurogenic, transsynaptic activity can turn on EOP gene expression as measured by increases in EOP mRNA and peptide levels. This transcriptional activation requires glucocorticoid steroids, which bind to a specific nucleotide sequence in one of the EOP genes. Current studies are examining how alterations in EOP gene expression, biosynthesis and release are linked to pain relief behavior in animals as a new approach to pain control. The mechanisms responsible for the development of tolerance to morphine and related opioid analgesics are not well understood. We have shown that the competitive NMDA (N-methyl-D-aspartate) receptor antagonist LY274614 can attenuate or reverse the development of tolerance to morphine's analgesic effects in animal models. The NMDA receptor system is involved in many of the changes that occur in the nervous system in response to alterations in sensory input. Some of the biochemical changes that occur with tolerance are the result of alterations in gene expression. We are using the ability of NMDA receptor antagonists to prevent morphine tolerance as a strategy with which to localize the biochemical and molecular changes that occur in tolerance. These studies are examining the EOP's and the recently cloned opioid receptors. We use the techniques of neuroscience and molecular biology including, cloning, Northern analysis and a new solution hybridization technique. Complementary clinical studies are aimed at defining the relationships between the disposition of analgesic drugs, and the effects of these drugs in patients with pain. These studies involve the development analytical methods and the application of computer based pharmacokinetics to clinical pain research with the goals of understanding how to maximize the therapeutic effects of these drugs while minimizing their adverse effects.

Dr. Kolesnick's research interests involve the description of a new signal transduction pathway termed the sphingomyelin pathway. In this cascade, activation of the 55 kDa TNF receptor or the 80 kDa IL-1 receptor initiates, within seconds, hydrolysis of sphingomyelin to ceramide by a neutral sphingomyelinase in the plasma membrane. Ceramide then acts as a second messenger, stimulating a membrane-bound serine/threonine kinase termed ceramide-activated protein kinase (CAPK), to propagate the signal. Recent investigations have identified CAPK as a 97 kDa autophosphorylating enzyme that is exclusively membrane-bound and Mg^{2+}-dependent.

Identification of downstream elements involved in signaling through this pathway has begun. Evidence has been provided that the sphingomyelin pathway mediates TNF activation of $p42^{mapk}$ and nuclear translocation of NF-κB in human leukemia (HL-60) cells. Further, the sphingomyelin pathway appeared solely responsible for replication of human immunodeficiency virus (HIV)-1 in an HL-60 cell model infected with 1 provirus per cell. This event is purportedly mediated by nuclear translocation of NF-κB. Recent studies showed that this pathway is responsible for TNF-induced apoptosis in a variety of cell lines known to respond to TNF with cytolysis. Ongoing studies are evaluating the role of this system in ionizing radiation-induced apoptosis and in cellular stimulation by bacterial lipopolysaccharide.

Since 1987 *Dr. Levi's* laboratory has been interested in the role of nitric oxide (NO) in cardiovascular physiology and pathophysiology. Recently, we have begun

investigating the molecular mechanisms by which NO and other vasoactive mediators, such as histamine, transmit signals. For this, we are elucidating G protein involvement in signal transmission initiated by NO which may lead to catecholamine and cytokine release from neural and lymphoid cells, respectively. Furthermore, we are assessing the role of histamine H_3-receptors in modulating norepinephrine release from sympathetic nerve endings in the mammalian heart, both in health and disease. Towards this end, we are characterizing cardiac histamine H_3-receptors and elucidating their signal transduction pathways. Other ongoing studies include an assessment of the role of NO in the vasorelaxant response of coronary arteries to low oxygen states, both in normal and atherosclerotic animal models. We are also examining NO synthase gene expression in blood vessels of genetically hypercholesterolemic animals and its correlation to atherosclerotic coronary dysfunction. Further, we are investigating signal transduction mechanisms in arterial smooth muscle cells and their derangement by abnormal cholesterol metabolism.

Dr. Levin is interested in understanding the physiological significance of signal transduction cross-talk. Adenylyl cyclase, the effector molecule of the cAMP pathway, is subject to regulation by other signaling systems. This presents a problem for maintaining the specificity of responses. The laboratory is investigating the various mechanisms of adenylyl cyclase regulation using a combined molecular and biochemical approach. Chimeras between differentially regulated forms of adenylyl cyclase can be used to identify important regulatory domains. Subsequent biochemical analysis will elucidate the molecular mechanisms of these modes of regulation.

The physiological importance of adenylyl cyclase regulation can be investigated using genetics. *Drosophila* homologs of mammalian isoforms will enable determination of the specific physiological roles of a regulatory mechanism. For example, the *Drosophila* learning and memory gene, *rutabaga,* like its mammalian counterpart, is regulated by the distinct second messenger calcium (CA^{2+}). The role of CA^{2+} regulation can be investigated by mutational inactivation of the CA^{2+} responsiveness of the *rutabaga* adenylyl cyclase *in vivo*.

Dr. Mendelsohn's laboratory is studying the epidermal growth factor (EGF) receptor from a number of points of view. (1) Exogenous and endogenous agents that control autophosphorylation of the EGF receptor are being investigated. These include SGF-α and TGF-α, as well as regulators of protein kinase C, activated receptors for other growth factors, and phosphatases. (2) The interactions between endogenous growth factors (autocrine loops) and other agents that promote or inhibit cell proliferation, including TGF-β and the interferons are being explored. (3) The laboratory has produced anti-EGF receptor monoclonal antibodies that inhibit EGF and TGF-α binding and block receptor activation. These are utilized in the above biologic experiments, and preclinical studies and clinical trials in patients are being carried out, exploring the capacity of antireceptor antibodies to act as antitumor agents. Conjugates of antireceptor antibodies with cytotoxic agents and radionuclides are under investigation in human tumor xenograft model systems.

Dr. Okamoto studies the neuropharmacologic bases of the drug dependence produced by centrally acting drugs in adults and neonates exposed to drugs during their fetal period. Central nervous depressant drugs, i.e. alcohol, barbiturates and benzodiazepines have been her major interest.

Electrophysiologic, neurochemical and behavioral effects are studied during acute and chronic drug treatment: functional and cellular mechanisms for the tolerance and dependence production are investigated: chronic effects of these drugs are studied on developing synapses and on the maturation of the nervous system.

Dr. Pasternak studies the pharmacology of opioid receptors at the molecular, cellular and systems level. The major focus is the identification and characterization both biochemically and pharmacologically of novel opioid receptor subtypes. In addition to traditional synthetic organic chemistry with structure-activity approaches, radioreceptor binding and second messenger studies, the laboratory has recently cloned and expressed a novel kappa$_3$ related opioid receptor. The functions of the new clone, as well as those encoding traditional mu, delta and kappa$_1$ receptor subtypes, are being defined using antisense strategies both *in vitro* and *in vivo*.

Dr. Prochaska's major research interests are geared toward the design and implementation of pharmacological strategies for the prevention of human cancer. Although the carcinogenic process can be disrupted at several points, many recognized anticarcinogens share in common the ability to induce Phase II detoxication enzymes. "Anticarcinogenic enzyme inducers" are present in the human diet, and may play an important role in modulating cancer risk. The laboratory is attempting to elucidate the molecular mechanisms for Phase II enzyme induction so that more potent and less toxic inducers can be identified. Moreover, we are examining the role of these compounds in diseases that increase cancer risk, with the goal that appropriate patient populations can be identified for chemoprevention trials.

Dr. Reidenberg pursues a fundamental question in clinical pharmacology, "Why do different people react differently to the same dose of the same medicine?" His program in clinical pharmacology addresses the question in several ways. Currently, he is studying the pharmacology of gossypol and bioflavonoids. This is to evaluate their mechanism for altering potassium metabolism. In addition, he has found efficacy for gossypol in some human cancers and is trying to determine the mechanism for its antineoplastic and antifertility effects through identification and characterization of a gossypol receptor.

Dr. Rifkind's interest in environmental toxicology has led to the investigation of the biochemical mechanisms of polychlorinated biphenyl (PCB) and dioxin toxicity. These compounds bind to a cytosolic receptor (Ah receptor) which controls the expression of a group of gene products including specific isozymes of cytochrome P-450. Dr. Rifkind's laboratory is studying the relationship of cytochrome P-450 to the diverse toxic manifestations of PCB and dioxins. These include weight loss, thymic involution, tumor promotion, and cardiac toxicity. Her laboratory recently discovered that the cytochrome P-450 induced by toxic PCBs and dioxins increases the metabolism of the endogenous membrane fatty acid, arachidonic acid, to epoxides and monohydroxylated products. These arachidonic acid metabolites have biologic activities consistent with involvement in PCB and dioxin toxicity. Current studies focus on (1) the role of arachidonic acid metabolism in PCB and dioxin toxicity and (2) the effects of dioxin induced changes in arachidonic acid metabolism on signal transduction pathways in heart and liver.

Dr. Roepe's research is focused on obtaining a molecular-level understanding of the structure and function of adenosine triphosphate (ATP)-coupled active transport systems, particularly multidrug resistance proteins (P-glycoproteins, or MDR proteins), which are involved in making tumor cells resistant to chemotherapeutics. In this effort the laboratory utilizes the tools of molecular biology, biochemistry and biophysics. Biophysical approaches include both solution and single cell-based fluorescence studies of transport phenomena. In particular, single-cell photometry methods have recently been used to analyze the transport of various ions in multidrug resistant tumor cells. Another major activity of the laboratory is recombinant DNA-based overexpression and subsequent reconstitution of membrane proteins, for more biochemical studies. Other

molecular biological studies include site-directed mutagenesis to define substrate binding sites, gene fusion studies to assess membrane protein topology and target gene disruption, and studies on the mechanisms of gene amplification.

Dr. Scheinberg evaluates immunologic approaches to the study and therapy of human leukemia and lymphoma. The overall goals of the Hematopoietic Cancer Immunochemistry Laboratory are to identify and understand the functions of specific cell surface molecules on normal and neoplastic hematopoietic cells and, if possible, to use these molecules as targets for immunotherapy. This includes identification of cell-surface targets, development of new immunotherapeutic agents, and phase 1 study of these new agents in patients at Memorial Hospital with an emphasis on the use of monoclonal antibodies (mAb) as pharmacologic agents for therapy of leukemia and lymphoma. MAb may be used pharmacologically as carriers of potent toxins or isotopes specifically to tumor cells, as direct mediators of immune cell killing via complement or regulators of growth via cell surface receptors. Most projects focus on applying these approaches to the therapy of human leukemia and lymphomas. Other projects seek to identify novel targets for immunotherapeutics. Currently being studied: (1) M195, an mAb to CD33, which is restricted to early myeloid progenitors and acute myeloid leukemia (AML) cells; this mAb is active in the treatment of AML; (2) the regulation of cell surface aminopeptidases on leukemia cells; (3) development of vaccines for leukemia and lymphomas.

Dr. Scotto's research efforts are directed at dissecting the regulation of transcription of the P-glycoprotein gene, whose product is expressed in a tissue-specific fashion and, when overexpressed, has been shown to be responsible for the development of multidrug-resistance in mammalian cells. The major questions they are addressing include: 1) What transcription factors are involved in determining the tissue-specific pattern of P-glycoprotein expression? 2) What alteration in the normal transcriptional control of this gene leads to its aberrant overexpression in multidrug-resistant tumors? 3) Does the transient induction of P-glycoprotein gene expression induced by certain environmental agents utilize the same DNA elements and transcription factors that are required for expression in normal cells? and 4) If differences in transcriptional regulation of the P-glycoprotein gene in normal vs. drug-resistant cells are determined, can they be exploited therapeutically in order to achieve selective tumor kill? Using both *in vivo* and *in vitro* model systems, they have recently identified several transcription factors involved in the modulation of P-glycoprotein gene expression, and are now beginning studies of the signal transduction system(s) involved.

Dr. Sirotnak's research focuses on (1) molecular targets and other cellular biochemical determinants important to selective antitumor action of various categories of cytotoxic antimetabolites; (2) cytoplasmic membrane transport of pharmacologic agents; (3) molecular mechanisms of acquired resistance of tumor cells to antineoplastic agents; (4) the regulation of folate and nucleoside transporter gene expression; and (5) the regulation of antifolate embolism at the level of q-gene expression.

Folates play a crucial role in the biosynthesis of macromolecules. Access of tumor cells to exogenous plasma folate is made possible by the existence in the cytoplasmic membrane of a specific high-affinity transport system. Using c-DNA probes and antibodies, the genetic regulation and molecular biology of this system are now being examined in models which constitutively overproduce or underproduce the transport protein and during induction of tumor cells to terminal maturation. Similar studies are underway examining the folate polyglutamylating enzyme, folylpolyglutamate synthetase.

Folate and nucleoside analogs effectively accumulate in tumor cells via plasma membrane systems normally transporting natural folates and nucleosides. To understand the selective antitumor action of folate and nucleoside analogs, studies are being conducted of the properties and multiplicity of their cellular membrane transport, their interaction with enzymic and macromolecular targets, their intracellular metabolic disposition and their pharmacokinetic behavior. Mechanisms of acquired resistance in tumor cells of these antimetabolites and other cytoxic agents at the level of their cellular membrane transport, metabolic disposition and enzymic targets and regulation of gene expression are studied. Further studies on multidrug-resistance related p-glycoprotein and an analogous efflux pump for folate analogues are also ongoing.

Dr. Szeto's research focuses on the development of novel opioid drugs as obstetrical analgesics. Opiate drugs, such as morphine and meperidine, are widely used for pain relief during labor and delivery. Their use, however, is associated with a variety of side effects in the mother, including sedation, hypotension and respiratory depression. In addition, these drugs have been shown to decrease fetal heart rate variability, and cause respiratory depression and abnormal behavior in the newborn. Opiate drugs may adversely affect the fetus directly as a result of placental drug transfer, and/or indirectly by altering the delivery of oxygen and substrates to the fetus. Two different approaches are being used in the design of opioid drugs with fewer side effects on the fetus and newborn. One approach is to minimize the extent of placental transfer by using opioid peptide analogs rather than the conventional alkaloids. The second approach is to take advantage of the multiple classes of opioid receptors, and try to separate analgesia from the other effects of the opioids. The overall research effort involves the rational design and synthesis of novel opioid peptides with high selectivity for the μ and the δ receptors, and with varying degrees of lipophilicity; determination of the pharmacokinetics of these peptide analogs in the mother and fetus; and the determination of the effects of these peptide analogs on hemodynamic, respiratory, metabolic and neuroendocrine control in the mother and fetus.

Dr. Toth's laboratory is interested in modeling diseases of the central nervous system in animals. The main approach is to generate knock-out and transgenic mice defective in certain gene functions and study the consequences of these alterations at the cellular, and molecular level. One direction is to study the serotonergic system and its involvement in disease. Disturbances in the serotonergic system occur in human disorders such as anxiety disorders and depressive syndromes. Another focus is to clone genes involved in epilepsy, and study how the dysfunction of these genes lead to neuronal hyperexcitability.

Dr. Watanabe has a broad interest in various facets of organic chemistry and biochemistry, especially in the development of new chemical reactions and their application to the design of novel molecules that exhibit anticancer and/or antiviral activity, or that are useful in elucidating enzyme reaction mechanisms. Many analogues of nucleic acid components and folic acid have been designed and synthesized using new chemistry developed in Dr. Watanabe's laboratory. Some of these compounds underwent clinical studies. Novel intercalating agents that bear covalent bond-forming capability have been synthesized, some of which showed potent activity against topoisomerases and many cancer cell lines.

More recently, Dr. Watanabe's group synthesized oligonucleotides containing modified nucleosides and their physico-chemical and biochemical properties studied. The basic knowledge obtained with the synthetic oligonucleotides will be applied in the development of antisense and antigene strategies for development of more selective anticancer and antiviral drugs.

Recent Publications

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Program in Physiology and Biophysics

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Research Activities

Physiology is the science of biological function, of how living things work, and research in physiology and biophysics combines the search for understanding function with a strong emphasis on quantitative precision. The members of the Graduate Program in Physiology and Biophysics study function at the molecular, cellular, organ, system levels using a wide variety of scientific disciplines that, in addition to physiology, include biochemistry, cell biology, computer modeling, molecular and cellular electrophysiology, molecular biology, neuroanatomy, neurophysiology and nuclear magnetic resonance. The research interests of the faculty are concentrated in central areas of physiology and biophysics, such as: the structure, function and regulation of integral membrane proteins, including ion channels and hormone receptors; intracellular electrolyte homeostasis, cell volume regulation, and renal function; mechanisms of hormone action, receptor turnover, and gene regulation; development and regeneration in the kidney and the nervous system; and radiation biology.

Dr. Andersen investigates structure and function of membrane proteins. These questions are addressed in experiments on membrane-spanning channels. At present, the following issues are under investigation: how do the primary amino sequences encode the conformation of membrane-spanning channels; how do individual amino acid residue substitutions modulate function; why can individual channels function in several distinct modes; and what are the mechanisms by which the host bilayer can modulate channel function? The primary techniques used in the lab include: single-channel and other electrophysiological measurements, kinetic analysis, and simulations.

Dr. Blanck's research interests include the effects of anesthetics on intracellular calcium distribution in cardiac and neuronal cells. These studies are designed to further the understanding of how volatile anesthetics work to produce general anesthesia, their protective effects during ischemia, and their depressive effects on cardiac contractility. These varied effects appear to share a common mechanism of action, at least in part, that being the alteration of calcium ion availability and fluxes. These changes are being studied by examining several calcium sensitive sites in cardiac and neuronal cells.

Plasma membrane calcium channel density is characterized by measuring the number and affinity of drugs binding sites in the presence of volatile anesthetics. Studies are under way to characterize the functional properties of single calcium ion channels which have been incorporated into artificial lipid bilayer membranes.

Dr. Duch's laboratory investigates the molecular interactions which define and control the functions of ion channels. This work reconstitutes purified and unpurified sodium channels from the electric organ of the electric eel and the human brain into planar lipid bilayers in order to probe the molecular interactions between the protein and non-protein (carbohydrate and lipid) domains of these channels. These interactions may play important roles in regulating channel function. In a related project, the mechanisms by which anesthetics modify ion channel function are being examined on a single channel level. These experiments, also conducted with sodium channels in planar lipid bilayers, are designed to probe the intermolecular interactions which define the anesthetic response.

Dr. Gardner combines neurophysiology with computer exploration of networks of simulated neurons to ask how the cellular and network properties of individual neurons give rise to the complex behavior of the brain. Recent neurobiological findings advance the ideas that postsynaptic neurons control synaptic strength by regulating the amount of neurotransmitter released upon them, that release is individually controllable at different terminals, and that this control is dynamically altered by the nervous system, producing a form of learning. Recent parallel investigations into artificial neural network models have developed a plausible neurobiological substrate for back-propagation, a major network learning rule.

Dr. Gershengorn's focus of research is to delineate the structure-function relationships of guanine nucleotide-binding (G) protein-coupled receptors (GPCRs). GPCRs regulate the function of virtually every cell in the body, are involved in some pathophysiologic processes and are the target site for therapeutic agents. We study two receptors that are activated by peptides, thyrotropin-releasing hormone (TRH), which regulates the anterior pituitary gland and acts in the central nervous system (CNS), and calcitonin, which regulates bone metabolism and acts in the CNS also. TRH and calcitonin bind to receptors on cell surfaces leading to activation of a G protein(s) that in turn activates an effector enzyme, a phospholipase C or adenylyl cyclase, or both. Using CDNAs that encode these receptors and techniques of molecular genetics, the structure-function relationships of hormone binding to its receptor and coupling of the receptor to the G protein, and mechanisms of regulation of receptor synthesis, internalization, down-regulation and degradation are being studied. Emphasis is placed on the use of receptors mutants and chimeras in these studies, and on molecular modeling of the hormone-receptor interactions. A second focus of research is the use of adenovirus-mediated gene transfer for basic studies of receptor biology and for gene therapy. Expression of exogenous receptors in mammalian cells is usually accomplished by transfection. However, transfection may yield low levels of receptor expression or restrict the range of cell types for expression. We are using adenovirus because a wide variety of cells are susceptible to gene transfer by adenovirus and the levels of expression attained are very high. Using adenovirus-mediated gene transfer, we are studying the differences in receptor biology observed in different cell types *in vitro*. And, we will use it for *in vivo* expression to extend these studies to animal models.

Dr. Grafstein's primary research interest is in nerve regeneration. At present, she is working to characterize the function of a prominent glycoprotein in goldfish brain that has been implicated in neuronal plasticity, including nerve regeneration and learning. Her studies have shown that the protein is primarily localized in non-neuronal cells,

including the meninges, outer wall of blood vessels and leucocytes. Thus this protein may play a role in the interaction between the nervous system and the immune system. Among the techniques used in Dr. Grafstein's laboratory are isotope tracer studies, high-resolution autoradiography, immunocytochemistry, electron microscopy and 2-dimensional gel electrophoresis.

Dr. Herzlinger's research program is focused on identifying the signals that enable embryonic cells to differentiate into the 14 different renal cell types required for normal kidney function. Utilizing the tools of molecular and cell biology her laboratory has characterized embryonic renal cells and determined the stage at which these cells assume unique differentiated fates. Future studies will now be aimed at identifying the signals and cellular mechanisms that mediate this developmental process.

Dr. Koutcher's research focuses on *in vivo* applications of nuclear magnetic resonance (NMR) to the study of hematologic and neoplastic diseases. These studies are performed in animal tumor models (mice), cell culture systems, and in patients. The focus of much of the work is to determine whether tumor metabolism, as monitored by *in vivo* NMR spectroscopy, can be used to (1) determine tumor sensitivity to antineoplastic therapy, or (2) to enhance treatment by optimizing the choice or timing of therapy based on changes in tumor metabolism. More recently ^{1}H volume localized spectroscopy has been used for the study of bone marrow in patients with hematologic diseases. These studies are being expanded to cell models.

Dr. Li's experiments have shown that of the many heat shock proteins (hsp's) preferentially synthesized after a heat shock, the concentration of hsp70 appears to correlate best with heat resistance, either permanent or transient. The long-term goal of her research project is to establish the molecular basis related to the role that hsp70 plays in modulating cellular responses to heat and drugs or other environmental stresses. Her current research emphasis is placed on the following: (1) To develop and characterize a model system to study the physiological functions, cellular targets and biochemical properties of hsp70 by mutagenesis of the cloned human hsp70 gene. Using the system developed, Dr. Li plans to study the structural domains and functions of hsp70. Specifically, she will address questions on what mutations in hsp70 gene will alter its biochemical properties, its cellular targets and/or physiological function(s). (2) To study of the role of hsp70 in protecting macromolecules or protein complexes from heat-induced denaturation (inactivation or insolubilization), using *in vivo* and *in vitro* model system; to investigate the structural domain of hsp70 responsible for this role. (3) To develop a practical assay using hsp70 as a means to predict and monitor heat resistance and thermotolerance in various cell lines and tissues. (4) The study of the interrelationships between heat response, thermotolerance, drug resistance, and heat-drug interaction.

Dr. Ling is interested in the biological effects of radiation pertaining to application to radiotherapy. Current interests include the mechanism of radiation-induced apoptosis and the effects of c-myc and Ha-ras oncogenes on apoptosis.

Dr. Lipkin's studies have been directed to measurements of abnormal stages of cell development that are associated with increased susceptibility to cancer. They include studies of abnormally proliferating and differentiating cells, and gene structure and expression during the evolution of neoplasms. The findings are applied to test mechanisms of action and potential utility of chemopreventive agents both in rodent models and in human subjects. The effects of specific nutritional modifications on colonic epithelial cell proliferation and differentiation are analyzed to guide the development of new classes of chemopreventive compounds, and to test their efficacy.

Dr. Maack's studies are directed to the elucidation of the physiology of cardiovascular hormones and their receptors as well as the organ and cellular processing of

peptide hormones and their receptors. In the past few years, the laboratory has been dedicated to the study of a novel polypeptide hormone, atrial natriuretic factor (ANF). Studies in the laboratory elucidated the structure of ANF as well as the main functional actions of the hormone on the kidney and cardiovascular system. More recently, the laboratory discovered that a main class of ANF receptors in kidney and vasculature is involved in the removal of ANF from the circulation and plasma homeostasis of the hormone. Studies are presently under way on the cellular physiology of ANF binding, internalization, lysosomal hydrolysis and on the recycling of ANF receptors in cultured cells. The techniques used in Dr. Maack's laboratory include studies in intact anesthetized and conscious rats, isolated perfused rat kidney, cell culture, receptor-hormone interactions, and general cell physiology and molecular biology techniques.

Dr. MacLeish's research program focuses primarily on the functional organization of the vertebate retina. Dissociated neurons from adult amphibian and prime retinae are employed to study the electrical properties of identified cells and the physiological properties of synapses formed among the retinal neurons *in vitro*. Voltage-sensitive dyes along with conventional intracellular recording techniques are used to measure electrical activity. A separate area of study is the trans-differentiation of retinal pigment epithelium into neural retina, a process that occurs in adult newts and salamanders. Antibody markers are being generated to describe the regeneration process in more molecular terms and a culture system is being refined to determine the role of soluble factors in regeneration.

Dr. Palmer's research focuses on the mechanism of transepithelial Na^+ and K^+ transport by tight epithelia, and the control of this process by hormones. The major effort is to define the nature of the Na- and K-selective channels responsible for the movement of these ions across the luminal cell membrane of epithelia, and to identify the intracellular events which modify the function of the channels. The experimental model being investigated in most detail is the rat renal cortical collecting tubule. Information about the functional properties of the channels and their regulation is obtained using electrophysiological approaches, especially single-channel and whole-cell current analysis using patch-clamp techniques. The molecular properties of the channels are also being investigated. Epithelial Na and K channels have recently been cloned and sequenced using expression cloning in *Xenopus* oocytes. The structure-function relationships of these channels are being explored using the approach of site-directed mutagenesis. Regions of the protein important in ion conduction and in channel gating and modulation are being mapped.

Dr. Pickering's main area of research is concerned with development of improved methods for the noninvasive measurement of blood pressure. First, he is using ambulatory monitoring techniques to learn more about the causes of blood pressure variability in normal and hypertensive subjects. This work has shown that most of the observed circadian rhythm of blood pressure can be accounted for by changes of activity and that blood pressure variability is an independent risk factor for coronary heart disease. Second, with Dr. Seymour Blank, he is analyzing the causes and origins of Korotkoff sounds with a view to the development of a new technique for blood pressure measurement.

Dr. Sackin's research interests have focused on the electrophysiology of renal epithelia. Recent work has utilized the patch clamp technique to study single channel and whole cell currents in the proximal tubule and collecting duct of the kidney, with particular emphasis on the role of stretch-activated ion channels. These mechano-sensitive channels alter their electrical gating properties as a function of membrane tension. They can act as micro-transducers that convert pressure and osmotic informa-

tion into electrical currents. This may be important for both volume regulation and electrolyte homeostasis. Experiments are also in progress using patch-clamp techniques to study renal potassium channels expressed in *Xenopus* oocytes.

Dr. Sealey's research addresses the question of the roles of renin gene expression in the kidney and reproductive organs. They investigate the mechanism whereby tissues that abundantly express the renin gene avoid interference with the circulating renin system in which very low levels of plasma renin are vital for maintenance of blood pressure. Dr. Sealey has evidence that the functions of tissue and circulating systems are separated by the actions of two different renins. Active renin continuously forms angiotensin in the circulation. Prorenin, previously thought to function primarily as biosynthetic precursor of renin, has been shown to have its own renin-like activity. Current research focuses on the idea that prorenin catalyzes tissue angiotensin formation when it binds to a receptor. This allows separation of the different effects of circulating and tissue renin systems. This work may lead to the development of specific pharmacologic agents enabling selective blockade of renin system at different target sites.

Dr. Silver's research involves intracellular Ca and pH both play extremely important roles in cellular homeostasis. The primary focus of his laboratory is studying intracellular pH regulation and variations in cytosolic Ca levels as they relate to peturbations in either acid-base state or fluctuations in ion transport in renal tubules and renal-related cell lines. Much of this work is performed in the cells comprising the cortical collecting tubule of the mammalian nephron. This segment of the kidney is primarily responsible for both acid base regulation and sodium and potassium balance. The interactions of intracellular Ca and pH as they relate to epithelial cells function are being studied using dual wavelength intracellular fluorescent pH and Ca indicators which are loaded intracellularly and monitored with photometric and digital imaging techniques. These indicators are unique in that when excited by the appropriate wavelengths of light they will give off photons and fluoresce relative to either the amount of ions bound to the dye or the free dye itself. These extremely powerful tools have allowed Dr. Silver to view dynamic changes in intracellular pH and Ca at the cytoplasmic level without disruption of cell function. Most recently he has specifically applied these techniques in investigating the functional activity of an ATPase that is responsible for hydrogen and potassium balance in the cortical collecting tubule. His future plans include applying the fluorescence biotechnology to look at the role of intracellular ions at the level of cell functions as it relates to cell structure.

Dr. Stephenson is interested in theoretical aspects of transport in biological systems. Much of his recent research centers on transport of water and electrolytes in epithelia and in the kidney. One group of current studies focuses on the relation of medullary concentration gradients and the osmolality of final urine in the mammalian kidney to tubular and vascular permeabilities, flows, and architecture. A second project is to develop a mathematical model of electrolyte transport in the whole kidney, which includes electrolytes (Na^+, K^+, Cl^-, HCO_3, H_2PO_4, H^+), glucose urea, protein osmotic forces, hydrostatic pressure, and electrical potential. Approaches to these problems include both computer simulation and the development and theoretical analysis of mathematical models.

Dr. Weinstein is interested in the theory of solute and water transport across epithelia and development of mathematical models that permit the computer simulation of normal and pathological conditions. The primary focus of this work is the study of the proximal tubule sodium reabsorption: the transepithelial pathways and driving forces of sodium transport and the mechanisms by which physical factors modulate this reabsorption. A second focus of this research has been the dynamics of cell volume

homeostasis, with scrutiny of proposed mechanisms for the coordination of solute transport at luminal and basolateral epithelial cell membranes. The most recent effort is the development of a mathematical model of the collecting duct, which will be used to simulate currently available clinical tests of distal nephron acidification.

Dr. Windhager's studies are aimed at elucidating the mechanisms of ion and water transport by renal epithelial cells, in particular the negative feedback regulation of sodium transport in cortical collecting tubules. Combining techniques of measuring transepithelial sodium fluxes, intracellular ion concentrations by fluorescence methods, and patch clamping of ion channels, it was concluded that cytosolic calcium ions and membrane voltage can account for the observed feedback control. In other studies, a new water channel (WCH-30kd) from the renal medulla that is independent of ADH has been expressed in *Xenopus* oocytes and has been fully cloned.

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Interdisciplinary Program in Molecular and Cellular Biology

Faculty

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Rosemary Bachvarova (Cell Biology & Genetics)
David M. Bader (Cell Biology & Genetics)
Francis Barany (Molecular Biology)
Robert Benezra (Cell Biology & Genetics)
Kenneth I. Berns (Molecular Biology)
Joseph R. Bertino (Pharmacology)
Carl Blobel (Cell Biology & Genetics)
Esther Breslow (Biochemistry & Structural Biology)
Anthony M. C. Brown (Cell Biology & Genetics)
Michael Caudy (Cell Biology & Genetics)
Moses V. Chao (Cell Biology & Genetics)
Bo Dupont (Immunology)
Erik A. Falck-Pedersen (Molecular Biology)
Donald A. Fischman (Cell Biology & Genetics)
Leonard P. Freedman (Cell Biology & Genetics)
Samuel E. Gandy (Neuroscience)
Marvin Gershengorn (Cell Biology & Genetics)
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Steven A. Goldman (Neuroscience)
Lorraine J. Gudas (Pharmacology)
Barry M. Gumbiner (Cell Biology & Genetics)
David P. Hajjar (Biochemistry & Structural Biology)
Ulrich Hämmerling (Immunology)
Ulrich F. Hartl (Cell Biology & Genetics)
Doris Herzlinger (Physiology & Biophysics)
William K. Holloman (Molecular Biology)
Alan N. Houghton (Immunology)
Jerard Hurwitz (Molecular Biology)
Maria Jasin (Cell Biology & Genetics)
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Elizabeth Lacy (Molecular Biology)
Janet S. Lee (Immunology)
Kenneth O. Lloyd (Immunology)
Peter MacLeish (Neuroscience)
Kenneth J. Marians (Molecular Biology)
Joan Massague (Cell Biology & Genetics)
Alton Meister
Takashi Mikawa (Cell Biology & Genetics)
Malcolm S. Moore (Cell Biology & Genetics)
Carl F. Nathan (Immunology)
Janko Nikolic-Zugic (Immunology)
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Jeffrey V. Ravetch (Molecular Biology)
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Hugh D. Robertson (Biochemistry & Structural Biology)
Enrique Rodriguez-Boulan (Cell Biology & Genetics)
James Rothman (Biochemistry & Structural Biology)
Kathleen W. Scotto (Pharmacology)
Stewart Shuman (Molecular Biology)
Roy L. Silverstein (Cell Biology & Genetics)
Kendall A. Smith (Immunology)
Mark Y. Stoeckle (Immunology)
Osias Stutman (Immunology)
Paula Traktman (Cell Biology & Genetics)
John A. Wagner (Neuroscience)

The Interdisciplinary Program in Molecular and Cellular Biology combines faculty members from the other seven programs of the Graduate School of Medical Sciences to provide broad-based training towards the PhD or MD-PhD degree in a variety of biomedical disciplines. Students are admitted "at large," i.e., without initial commitment to one of the school's more specialized fields of study. The program has been designed to give the student both a comprehensive understanding of the cellular and molecular basis of life processes and the background and training necessary for independent research.

For a description of research activities and recent publications of the participating faculty members, see under the programs indicated in the faculty list above.

Requirements and Course Offerings

Memorial Sloan-Kettering Cancer Center and Manhattan Skyline, as seen from Cornell Medical College.

Admission

Applications

Applications to the Cornell University Graduate School of Medical Sciences are accepted for the degree of Doctor of Philosophy and, under special circumstances, the degree of Master of Science. An applicant must (1) have a baccalaureate degree or the equivalent from a college or university of recognized standing, (2) have adequate preparation in the chosen field of study, and (3) show promise of ability to pursue advanced study and research, as judged by his or her previous record.

As a rule, students are admitted to one of the following programs: *Biochemistry and Structural Biology, Cell Biology and Genetics, Immunology, Molecular Biology, Neuroscience, Pharmacology, and Physiology and Biophysics,* or to the *Interdisciplinary Program in Molecular and Cellular Biology.* However, the initial affiliation with a program is far from rigid. For example, a student, after developing an awareness of the variety of research projects available for training, may remain in the original program but choose as thesis advisor a faculty member affiliated with another program, or the student may wish to change programs altogether.

Inquiries about graduate study should be addressed to the Associate Dean of the Graduate School of Medical Sciences, 445 E. 69th Street, New York, NY 10021 [Telephone: (212) 746-6565; Fax (212) 746-8906.]

Candidates may be admitted in September, February, or July, although places in the graduate program for February and July may not be available because of prior commitments to applicants for September admission. Applicants for February or July admission should correspond directly with the respective Program Director regarding the availability of places.

Application material must be completed and returned to the Office of the Graduate School of Medical Sciences together with (1) official transcripts of records from all colleges and universities attended, (2) a statement of purpose of graduate study, and (3) two letters of recommendation from individuals in academic positions who know the applicant professionally. In addition, scores from the Graduate Record Examinations (GRE) are required to aid in the evaluation of an applicant. Application for taking the Aptitude (Verbal, Quantitative, and Analytical) Test and the Advanced Test of the GRE, must be made directly to the Educational Testing Service, Graduate Record Examinations, P.O. Box 6000, Princeton, NJ 08541-6000. Students whose native language is not English are required to take the Test of English as a Foreign Language (TOEFL). Application for this test must be made to Test of English as a Foreign Language, P.O. Box 6151, Princeton, NJ 08541-6151.

The proper Institution Code Number to use in the GRE or TOEFL application for the Cornell University Graduate School of Medical Sciences (New York City) is R 2119.

Applications for September or July admission and all credentials, including official transcripts of records from all colleges and universities attended, must be received by the **deadline of January 15.** Because GRE scores are an important part of the application it is of decided advantage to the applicant, to submit these scores by the January 15 deadline.

Applications and credentials for February admission must be received by November 1.

Application fee. A nonrefundable charge of $50 is made for filing an application for admission.

The completed application and all supporting documents are initially screened by the credentials committee of the program to which the student is applying. Applicants who are considered potentially acceptable are usually called for a personal interview. If accepted by the Program, an application is forwarded to the Dean for final decision. A student is formally notified of acceptance for study in the Graduate School of Medical Sciences by a letter from the Dean. An applicant accepted for admission is requested to promptly inform the Graduate School of Medical Sciences of her or his plan to either accept or refuse the offer of admission.

It is the policy of Cornell University to actively support equality of educational and employment opportunity. No person shall be denied admission to any educational program or activity or be denied employment on the basis of any legally prohibited discrimination involving, but not limited to, such factors as race, color, creed, religion, national or ethnic origin, sex, age, or handicap. The University is committed to the maintenance of affirmative action programs which will assure the continuation of such equality of opportunity.

Admission policies are also in conformity with the policy of New York State in regard to the American ideal of equality of opportunity as embodied in the Education Practices Act.

Special Students

Special students are students who are not degree candidates in the Graduate School of Medical Sciences and who are given permission by the Dean to take courses at Graduate School of Medical Sciences. Special students must be degree candidates at other institutions and the courses taken at Cornell must be essential to their degree programs and are not offered by the institutions in which they are matriculated as degree candidates, as certified by the institutions. Enrollment as a special student is not intended as preparation for admission to degree programs at Cornell or elsewhere.

Special students are accepted only with the approval of the appropriate Program Chairperson. Such students must demonstrate special qualifications in terms of preparation and ability. They must register with the Graduate School of Medical Sciences and must pay all tuition and fees before being permitted to attend lectures or laboratory sessions. Tuition is computed on the basis of the ratio of course hours taken to the total hours of instruction for the academic year (33 weeks of 40 hours). There is a registration fee of $35.

Degree Requirements

Major and Minor Programs

A candidate for the degree of Master of Science is required to register for study in one major and one minor program. Each program decides whether the Special Committee of a candidate for the PhD degree must have two or three programs represented. Accordingly, a candidate for the degree of Doctor of Philosophy is required to register for study in one major and one or two minor programs. At least one of the minors must be outside the area of the major program.

The Special Committee

The general degree requirements of the Graduate School of Medical Sciences are minimal in order to give maximum flexibility in choosing a desirable program of study. The student's program is determined with the aid and direction of a Special Committee, consisting of at least three faculty members chosen by the student from those programs that best fit his or her areas of interest. At least one member of the committee must represent a program different from the candidate's major program. Satisfactory progress toward a degree is judged by the committee rather than by arbitrary standards imposed by the Graduate School of Medical Sciences. There are no regulations of the Faculty of the Graduate School of Medical Sciences governing the specific content of instruction, courses, or grades to which the Special Committee must subscribe, except those imposed by the programs. The committee is primarily responsible for the candidate's development as an independent scholar and scientist.

The major sponsor usually advises the student concerning the selection of other committee members and chairs the committee. Members may agree to serve temporarily during the candidate's first year of residence until the candidate has had the opportunity to become acquainted with areas of research in the programs of his or her choice. On completion of this year of residence, a permanent Special Committee will be formed, the membership of which can be changed with agreement of all members of the old and newly formed committees and the approval of the Program Chairperson or Director. The members of the Special Committee decide on the student's program of study and research. They judge whether progress toward a degree is satisfactory and prepare term reports on the candidate for submission to the Dean. The members of the committee serve on all the candidate's examining committees and they approve his or her thesis.

The formation of a permanent Special Committee requires the submission by the student of a Nomination of Special Committee form to the Graduate School Office. (The Nomination of Special Committee form must be on file for a student to schedule the Admission-to-Doctoral Candidacy Examination.)

Registration and Course Grades

No student in the Graduate School of Medical Sciences may double-register for an advanced general or professional degree with any other school or college except the Cornell University Medical College.

At the beginning of each term, students are required to register with the Office of the Graduate School of Medical Sciences and to file a registration of courses form indicating all courses they will take. A fee of $10 is charged for late registration.

At the beginning of each course in which the student is enrolling, the student will complete a separate course registration form for the instructor. All courses for which the student registers for credit will be entered in the official record. Grades of graduate students are reported as: Excellent (E), Satisfactory (S), Unsatisfactory (U), Incomplete (I), Absent (Abs), Unofficially Withdrawn (W) or Audit (Aud). A grade of Incomplete or Absent cannot be changed later than one term following the term in which the course was taken.

Registration for the summer is required of graduate students who will be engaged in research.

Residence

The Faculty of the Graduate School of Medical Sciences regards study in residence as essential. Each candidate for an advanced general degree is expected to complete the residence requirements with reasonable continuity. A student must register each term from the time of his or her first registration in the Graduate School of Medical Sciences until the student either withdraws or completes a degree (unless a leave of absence has been granted). Full-time study for one-half academic year with satisfactory accomplishment constitutes one residence unit. Two units of residence are the minimal requirement for the masters degree and six units are the minimum for the doctoral degree. However, the time necessary to obtain the degree generally exceeds the minimal requirements. A candidate for the PhD degree must spend two of the last four units of required residence in successive terms on the New York City or the Ithaca campus of Cornell University. No more than seven years may intervene between the time of first registration and the completion of all requirements for the doctoral degree. A student must complete all requirements for the master's degree in four years.

Part-time graduate study, if it is necessitated by off-campus employment noncontributory to the major program of study, is not encouraged. Requests for part-time study must be reviewed by the Executive Committee. If permission is granted for part-time study, the student must be in residence at least half-time.

Transfer of Residence Credit

No residence credit will be granted for study outside the Graduate School of Medical Sciences to fulfill the requirements of the MS degree. No commitment can be made about granting residence credit toward the PhD requirements for previous study in another graduate school until after the candidate has entered into residence at the Graduate School of Medical Sciences. At that time, the student's Special Committee may recommend acceptance of study outside the Graduate School of Medical Sciences to the Executive Committee, which will determine the number of residence units to be awarded. No credit can be transferred for study undertaken as an undergraduate or as a special student even in courses designed for graduate students.

A student who has satisfactorily completed two or more academic years of study toward the MD degree at the Cornell University Medical College, or another accredited medical school in the United States with a curriculum equivalent to that of the Cornell University Medical College, may transfer a maximum of two units of residence credit after passing an evaluation examination administered by a committee appointed by the Executive Committee of the Graduate School of Medical Sciences.

Summer Research

Registration is required for the summer research term whether or not this effort will be credited toward residence unit accumulation. Students registered for summer research pay prorated tuition only if they are obtaining residence credit. However, no degree candidate is eligible for more than two residence units in any period of twelve consecutive months.

Study *In Absentia*

A candidate for the degree of Doctor of Philosophy may petition for permission to earn residence units for study away from Cornell University while regularly registered in the Graduate School of Medical Sciences. A candidate to whom this privilege has been granted, must register as a Candidate *in absentia* and may work temporarily under the immediate supervision of an individual designated by his or her Special Committee although the candidate's program will continue to be directed by the Committee. For study *in absentia* not more than two residence units may be earned toward fulfillment of the minimal residence requirements for the PhD degree.

Leave of Absence

A candidate who finds it necessary to interrupt the continuity of his or her residence must petition the Dean for an official leave of absence. This written petition must specify the term of absence, state the reason for the requested leave of absence, and be approved by the student's major sponsor.

Candidacy for Degree Only

A graduate student who has fufilled all degree requirements, with the possible exception of the final thesis submission, and is no longer a full-time student, is granted Candidate for Degree Only status, which is in effect until graduation.

Examinations

Three examinations are required by the Faculty of the Graduate School of Medical Sciences: (1) Final Examination for the MS degree, (2) Examination for Admission to Doctoral Candidacy, and (3) Final Examination for the PhD degree. Examinations are administered by an Examining Committee consisting of a chairperson appointed by the Dean, the members of the candidate's Special Committee, and, in the case of the Admission to Doctoral Candidacy Examination, one additional member selected from the Faculty of the Graduate School of Medical Sciences or of other institutions. In addition to these examinations, the candidate's major program may require a qualifying examination as part of its evaluation of the candidate after two units of residence have been completed.

For the MS degree: The Final Examination may be oral or both oral and written.

For the PhD degree: The Admission to Doctoral Candidacy Examination is both oral and written and certifies that the student is eligible to present a thesis to the Faculty of the Graduate School of Medical Sciences. The examination should be taken after course work is largely finished but before significant thesis research has begun. Accordingly, the usual examination time will be at the end of the second year of residence. The examination may not be taken until two units of residence credit have been accumulated and a minimum of two units of residence credit is required after passing this examination before the final examination can be scheduled. The final examination for the PhD degree is an oral defense of the candidate's thesis. It must be passed within four years after completion of the required residence units, or within seven years from the date of first registration, whichever is earlier.

A student preparing to take an examination must submit a completed Application for Examination form to the Graduate School Office approximately two months prior to the written portion of the Admission-to-Doctoral Candidacy Examination and at least one month prior to the Final Examination.

Thesis

A principal requirement for both the MS and the PhD degrees is the presentation of a thesis constituting an original contribution to knowledge. Ordinarily, the thesis is written on a research topic in the candidate's major field of study, under the direction of the chairperson of his or her Special Committee. The time between the thesis defense and submission of the thesis in its final form is limited to 60 days. The faculty requires that the PhD thesis be published in abstract and be recorded on microfilm.

Tuition and Fees

Tuition

Tuition for a student regularly matriculated in the Graduate School of Medical Sciences is $16,000 for the academic year 1994–95. Tuition includes fees for matriculation, the student health plan, graduation, and miscellaneous thesis expenses.

Students in the PhD-MD program (see pp. 4 and 72) will be charged Medical College tuition while they are enrolled in medical school.

A student who is to receive partial residence credit (see p. 66) because of employment should apply for proration of tuition on forms obtainable at the Office of the Dean.

Other Fees

In Absentia. A student registered *in absentia* pays a fee of $200 each term.

Leave of Absence. Students on leave of absence will be required to pay an active-file fee of $200 for each semester, up to a maximum of six semesters, during which they are not registered with the Graduate

School. This fee will not be subject to finance charges but must be paid before the student can receive an advanced degree. Petition for waiver of this fee will be considered for students who have not completed the required number of residence units.

For students on leave of absence, the student health plan will remain in force for 30 days following the commencement of the leave.

Candidacy for Degree Only. A student who registers as a Candidate for Degree Only pays a one-time fee of $35.

Any individual who owes money to the University will not be allowed to register or reregister in the University, receive a transcript of his or her record, have his or her academic credits certified, be granted a leave of absence, have a degree conferred, and will not be eligible for health services and subsidized housing.

The amount, time, and manner of payment of tuition, fees, or other charges may be changed at any time without notice.

Refunds

Part of the *personally* paid tuition will be refunded if the student obtains official certification of leave of absence or withdrawal from the Graduate School of Medical Sciences during the semester. Students who terminate their registration during a regular term in this manner will be charged tuition from the registration day to the effective date of the certificate as follows: first week, 10 percent; second week, 20 percent; third week, 30 percent; fourth week, 40 percent; fifth week, 60 percent; sixth week, 80 percent; seventh week, 100 percent. No charge will be made if the effective date of leave or withdrawal is within the first six days of the term, including registration day.

Financial Assistance

Students who wish to apply for a Stafford Student Loan or other Federal assistance are required to submit a Free Application for Federal Student Aid (FAFSA) for an estimate of financial need. Application forms can be obtained from the Graduate School Office.

Financial assistance is available to qualified applicants. Individual programs may offer predoctoral research fellowships, research assistantships, or teaching assistantships. These positions may provide a stipend in addition to tuition. Information about these positions may be obtained directly from the Program Director at the time of application.

Nationwide competitive predoctoral fellowships are available from the National Science Foundation, the National Research Council, and the Howard Hughes Medical Institute. Information about these fellowships should be requested directly from the appropriate agency.

New York State residents are eligible for several predoctoral fellowships and the Tuition Assistance Program. Application forms may be obtained from the New York Higher Education Services Corporation, Student Financial Aid Section, Tower Building, Empire State Plaza, Albany, NY 12255.

Several other loan programs are available to graduate students. Under these programs, repayment of the principal amount of the loan together with the interest on the loan may be deferred until after graduation. Complete information regarding loan programs may be obtained from the Graduate School Office.

Opportunity for part-time employment is often available in departmental research projects or other activities. Applications should be made directly to individual departments.

Scholarships and Fellowships

Full fellowships are available for graduate students. Recipients become PhD Fellows and are awarded a full tuition scholarship and a stipend covering living expenses. Tuition scholarships are available for students who are not covered by a fellowship. Scholarships and fellowships are administered by the Office of the Dean of the Graduate School of Medical Sciences.

In addition, the following named funds provide support for selected students:

The Vincent Astor Scholarship Fund. Funds for tuition assistance are also derived from the income from a generous gift by the Vincent Astor Foundation to the Graduate School of Medical Sciences and to the

Medical College. Allocation of these funds for graduate student tuition assistance is made at the discretion of the Dean of the Graduate School of Medical Sciences.

The Departmental Associates Fellowship was established by the generous contributions of The New York Hospital-Cornell Medical Center Departmental Associates for the support of a PhD candidate in the Cornell University Graduate School of Medical Sciences.

Herbert and Lee Friedman Fellowship provides support for an MD-PhD student and is funded through income derived from an endowment established by Mr. Herbert Friedman to the Sloan-Kettering Institute.

Lee Friedman Memorial Fellowship. Funds for the support of an MD-PhD student are provided by income generated from an endowment to the Sloan-Kettering Institute in memory of Lee Friedman, the wife of Herbert Friedman.

The Harry E. Gould, Sr., Medical and Graduate Student Scholarship. This fund was established by Mr. Gould's son, Harry E. Gould, Jr., in memory of his father, a prominent business and civic leader in the City of New York who had a long-standing interest in medicine. The income from this endowment provides financial assistance for students of the Medical College and Graduate School of Medical Sciences.

The Mildred and Emil Holland Scholarship. Income from a gift by the Emil and Mildred Holland Philanthropic Fund of the Jewish Communal Fund is used to provide tuition support for an MD-PhD student.

The Frank L. Horsfall, Jr., Fellowships are derived from income generated by the Frank L. Horsfall Jr. Fund and are awarded each year to two outstanding students sponsored by faculty members of the Sloan-Kettering Institute.

Robert W. Johnson, Jr., Charitable Trust. The income on a permanent endowment to the Sloan-Kettering Institute provides a fellowship for an MD-PhD student.

The W. M. Keck Foundation Medical Scientist Fellowship. This award is derived from a generous endowment awarded to Cornell University Medical College and provides support for an MD-PhD student.

The Frances L. Loeb Medical Scientist Fellowships. These fellowships have been endowed by a gift from Frances L. Loeb and provide support for two MD-PhD students at the Cornell University Medical College.

The Shirley L. Marshak Fellowship is funded by income derived from the Shirley L. Marshak Trust for Charities. The fellowship has been designated for award to a student of the Graduate School of Medical Sciences who is engaged in biomedical research.

The Andrew W. Mellon Foundation Fellowships. A grant by the Andrew W. Mellon Foundation provides fellowship support for MD-PhD students selected for the Tri-Institutional Medical Scientist Training Program which is administered jointly by Cornell University Medical College, the Cornell University Graduate School of Medical Sciences, and The Rockefeller University.

The Frank R. and Blanche A. Mowrer Memorial Fund. Financial assistance is available from the income of this fund to one student each year enrolled in the PhD-MD or MD-PhD program.

The Papanicolaou Medical Scientist Fellowship is funded by income from a bequest from Mary G. Papanicolaou in memory of her husband, Dr. George N. Papanicolaou, and by a gift from an anonymous donor to the Cornell University Medical College. The funds provide support for an MD-PhD student.

The Abby Rockefeller Mauzé Medical Scientist Fellowship was established by a gift from the Abby Rockefeller Mauzé Trust. The income provides fellowship support for an MD-PhD student.

Louis and Rachel Rudin Foundation. The generous gift to the Sloan-Kettering Institute from the Foundation provides a fellowship for an MD-PhD student.

Jack and Susan Rudin Educational and Scholarship Fund. Selected PhD students will be named Jack and Susan Rudin Scholars in the Biomedical Sciences and will be funded by this generous gift to the Sloan-Kettering Institute.

The Surdna Foundation Medical Scientist Fellowship was made possible by a

generous grant to the Medical College by the Surdna Foundation. The income from this endowment provides fellowship support for an MD-PhD student.

The Iris L. and Leverett S. Woodworth Medical Scientist Fellowship. Funds for the support of an MD-PhD student are provided by the income from a generous gift from Dr. Leverett S. Woodworth in his own name and in memory of his wife, Iris L. Woodworth.

The Marcus M. Reidenberg Gateways to Science Program. With generous funding by the Departmental Associates of the New York Hospital-Cornell Medical Center, the Cornell University Graduate School of Medical Sciences has implemented a program which will provide minority college students with summer research opportunities in laboratories of Cornell University Medical College and the Sloan-Kettering Institute. The aim of the program is to foster an interest in biomedical research in minority students at all college levels. The grant enables the school to provide a two-month stipend and subsidized housing for qualified students.

DeCamp Tri-Institutional Neuroscience Fund. Due to the generosity of the DeCamp Foundation, a fund has been established to promote neuroscience activities at Cornell University Medical College, The Rockefeller University, and the Sloan-Kettering Institute for Cancer Research. The gift supports an annual research symposium and a monthly graduate student research dinner.

Awards and Prizes

The Julian R. Rachele Prize. The income of a fund established by Dr. Julian R. Rachele, former Dean of the Cornell University Graduate School of Medical Sciences, provides for an annual prize to be awarded to a candidate for the PhD degree for a research paper of which the candidate is the sole or the senior author.

The prize was awarded in 1994 to Hernan Flores-Rozas.

The Vincent duVigneaud Prizes for the presentation of outstanding papers by students of the Cornell University Graduate School of Medical Sciences at the Annual Vincent duVigneaud Memorial Research Symposium.

Recipients of these awards in 1994 were David Circle, Victor Hatini, Alan Packer, Sandra Ryeom, Scott Schlemmer, Cynthia Smith, and Killu Tougu.

Student Health Services

The student Health Plan of Cornell University Medical College provides hospitalization and major medical insurance for all registered graduate students. In addition, the Plan provides for ambulatory care at the Student Health Service of The New York Hospital Cornell Medical Center. Physicians at the Health Service will refer students who require specialized care to clinics of the New York Hospital and to attending physicians when needed.

The cost of medical services provided by the Plan is included in the tuition and fee structure announced by the Graduate School of Medical Sciences each academic year. Students will be issued Plan membership cards and will receive courtesy privileges at The New York Hospital Pharmacy.

Entering students are requested to have a physical examination, tuberculosis skin test and laboratory tests performed by their personal physicians prior to matriculation. The hours of the Student Health Service and a complete statement of Plan benefits will be provided to each graduate student upon arrival.

Coverage of eligible dependents is included in the tuition and fee structure of the Graduate School of Medical Sciences. Insured dependents are eligible for care at the Student Health Service and will be referred to appropriate members of the Hospital staff for medical treatment.

Students who withdraw from the Graduate School of Medical Sciences will be covered for 30 days from the effective date of withdrawal. Dependent coverage may also be continued for this period, and costs will be prorated from the date of termination. See the Student Accounting Manager of the Medical College to make such arrangements.

Students on an academic leave of absence from the Graduate School of Medical Sciences will be covered for 30 days after the official commencement date of the leave. Dependent coverage may be continued for this period, and costs will be prorated from the date of termination. Students on medical leave of absence from the Graduate School of Medical Sciences will be fully covered for the duration of the academic year.

Graduating students and their dependents are covered until the last day of the month following the month in which the student was last registered in the Graduate School of Medical Sciences.

Residence Halls

F. W. Olin Hall, a student residence, is at 445 East Sixty-ninth Street, directly across from the Medical College entrance on York Avenue. Olin Hall contains a gymnasium, lounges, a kitchen on each student floor, and 185 residence rooms. Each room is a single bedroom-study, completely furnished. Two adjacent rooms share a connecting bath. The housing fee for the 1994–1995 academic year is $307 per month.

Livingston-Farrand Apartments, also located on East Sixty-ninth Street, just beyond Olin Hall, have furnished studio, one-bedroom, and two-bedroom apartments. Kitchen facilities are provided in these apartments. Housing fees begin at $432 per month (utilities not included). These apartments are available to families and upper-class students.

Jacob S. Lasdon House, an apartment residence, is located at 420 East Seventieth Street. This building contains studio, one- bedroom, and two-bedroom apartments, and two squash courts. Apartments are fully furnished, include kitchens, and are centrally air conditioned. Housing fees for students sharing apartments begin at $380 per month including utilities. Fees for families begin at $655 including utilities. These apartments are available to families and upper-class students.

303 E. 71st Street Apartments. A limited number of furnished apartments, operated by the Memorial Sloan-Kettering Cancer Center, is available for students of the Cornell University Graduate School of Medical Sciences. Rental rates are $752 and $1022 for one- and two-bedroom apartments, respectively, and utilities are included.

Housing in the above facilities is guaranteed for a five-year period from the time of first enrollment.

The fees listed may be changed at any time without previous notice.

Pets are not permitted in student housing.

Campus Security

Cornell University Medical College and Graduate School of Medical Sciences annually distribute a campus security report to all students and employees which contains descriptions of policies and procedures for reporting crimes and emergencies and campus crime data. The report lists telephone numbers and contact information for security in campus facilities and residences. Policies and procedures for handling sex offenses and programs for victims are also described. Copies of the current annual security report are available to prospective graduate students upon request to the Graduate School Office.

Special Programs

Application to the Tri-Institutional MD-PhD Program

See pp. 3 and 87 for descriptions of the program. A successful applicant will demonstrate excellent undergraduate science preparation and a strong commitment to combining an investigative career in the biomedical sciences with clinical medicine. Applicants must satisfy the requirements of each institution. After initial screening, selected candidates will be invited to meet with members of the faculties of the medical and graduate programs.

To complete an application, students must submit the following:

To AMCAS in Washington, D.C.:

1. *AMCAS Application.* A completed AMCAS application form should be sent directly to AMCAS by October 15. The personal data and academic record required are suitable for evaluation by both the medical and graduate schools.

To the Tri-Institutional MD-PhD Program, Cornell University Medical College, 1300 York Ave., New York, NY 10021:

2. *MD-PhD Application Form.* The Tri-Institutional Program Application Form will be sent when information about the program is requested.
3. *Test Scores.* MCAT scores are required; GRE scores are optional.
4. *Personal statement.* Candidates should submit a personal statement summarizing their research background and scientific interests, as well as reasons for wishing to pursue the combined degree.
5. *Letters of Recommendation.*
   a. Each applicant should arrange to provide either a statement and supporting material from his or her premedical

advisory committee, or two letters from undergraduate science faculty members evaluating the candidate's suitability for a career in medicine.
b. Letters from at least two faculty members evaluating the candidate's research potential should also be submitted.

6. *Application Fee.* A processing fee will be requested when the AMCAS application is received by the Medical College Office of Admissions. This fee can be waived in cases of financial hardship. There is no additional application fee for the MD-PhD Program.

Deadline. Applications must be received by **November 30.**

Application to the PhD-MD Program

See p. 4 for a description of the program. Students admitted to the program will matriculate as second-year medical students, following successful completion while enrolled in the Graduate School of Medical Sciences (GSMS) of all first-year courses of Cornell University Medical College (CUMC) and of all requirements for the PhD degree.

Application for admission to CUMC can be made either during the academic year preceding the year of anticipated enrollment, or two years prior to enrollment. Students must have passed the Admission-to-Doctoral-Candidacy Examination and at least two major first-year medical school courses by the time application is made. Admission, if granted, will be conditional pending completion of all requirements for the PhD degree and of all remaining first-year medical school courses.

To complete an application, students must submit, **by October 15,** the following documents to the Office of the Dean of the GSMS:

1. A completed application for admission with advanced standing (second year) to CUMC. Application forms are obtainable from the CUMC Admissions Office.
2. An up-to-date transcript from the GSMS showing successful completion of at least two *major* courses of the first-year medical school curriculum (Biochemistry, Gross Anatomy, Cell Biology and Microscopic Anatomy, Physiology and Biophysics, Neuroscience).
3. A plan of study for the remaining years in graduate school, incorporating all courses of the first-year medical school curriculum still to be taken. The plan must show endorsing signatures of the members of the student's Special Committee.
4. Two letters of recommendation, one by the student's major sponsor, and one by another member of the faculty of the GSMS addressing the applicant's suitability for PhD-MD program.
5. Results of the Medical College Admissions Test (MCAT).

The Office of the Dean of the GSMS will review the student's credentials and make a recommendation to the Committee on Admissions of CUMC. After review of the application and personal interviews, this committee will determine the acceptability of the student for the MD-PhD program and will inform the student of its decision before June 1.

After completion of the second and third years and the required selectives of the fourth year of the Medical College, students in the program receive credit for their graduate studies to satisfy the elective requirements of the fourth-year Medical College curriculum.

While registered as graduate students, the PhD-MD candidate is subject to the tuition schedule of the GSMS. Upon registration at CUMC, the candidate is responsible for the tuition charged by the Medical College (full tuition for the second and third years, and a minimum of 30% of the fourth-year tuition).

Core Curriculum

Cell Structure and Function. The objective of this interdisciplinary core course is to present entering graduate students with the basic concepts in biochemistry, cell biology, and molecular biology essential for each of the PhD programs in the graduate school. The course provides the foundation necessary for more specialized courses designed to meet the particular needs of each student.

The sixteen-week course, which is required for all incoming graduate students, is given during the first and second quarters of the academic year and has the following components: (1) lectures (four hours per week), (2) small-group discussions (two hours per week), and (3) "Frontier Seminars" (one hour per week).

Three factors will determine each student's grade: (1) Tests which will be given during the exam week of each of the two quarters. The two tests will each count 25% of the final grade. (2) Discussion (25% of the final grade). A student's participation in small-group discussions will be evaluated. (3) Research Proposal (25% of final grade). Each student will write a proposal on a topic presented in the course, including a review of current literature and an experimental protocol.

The teaching faculty for the course is drawn from all programs in the graduate school. Course director: Dr. Bader.

Biochemistry and Structural Biology

Graduate Program Chairpersons

Esther M. Breslow, Department of Biochemistry, Cornell University Medical College, Room E-219, 1300 York Avenue, New York, NY 10021, (212) 746-6405

Dinshaw J. Patel, Cellular Biochemistry & Biophysics Program, Sloan-Kettering Institute, 1275 York Avenue, New York, NY 10021, (212) 639-7207.

Graduate Program Director

David P. Hajjar, Department of Biochemistry, Cornell University Medical College, Room A-626, 1300 York Avenue, New York, NY 10021, (212) 746-6470

Graduate instruction is offered leading to the PhD degree. Within the framework of degree requirements and in consultation with the student, the course of study is planned to fit the need of the individual. Although formal course work is required, emphasis is placed on research. Research opportunities exist in various areas of biochemistry including enzymology, structure and function of proteins and nucleic acids, molecular biology, physical biochemistry, protein trafficking and peptide chemistry. Entering graduate students rotate for periods of two or three months in the laboratories of different faculty members of the Program before beginning their thesis research. Students are encouraged to choose challenging fundamental research problems that are on the frontiers of biochemistry and structural biology.

The laboratories of the faculty members are equipped with the instrumentation required for modern biochemical research. Graduate students are instructed in such methodology as high performance liquid chromatography, protein sequencing and amino acid analysis, recombinant DNA technology (including nucleic acid sequencing and the polymerase chain reaction), radioactive isotope techniques, crystallography, electrophoresis, circular dichroism, NMR and other spectroscopic methods.

Students who undertake graduate study in biochemistry and structural biology must have a sufficiently comprehensive background in general and organic chemistry to pursue the proposed course of study and must present evidence of knowledge of biology, general experimental physics, and mathematics.

Students may remedy deficiencies in these areas during the summer before entering graduate school, or in some cases, during the first year of graduate study. The Graduate Record Examination (the aptitude test and the advanced test in chemistry or biochemistry) is ordinarily required.

Course requirements: In the first year students take the core course (see p. 73) for graduate students given in the first two quarters. In addition, all students are required to participate in Journal Club. No other courses are required, but graduate students are generally encouraged to select additional courses in biochemistry, in their minor program, or in other programs, in consultation with the members of their Special Committee. Students in the MD-PhD program are required to complete the first two years of the medical school curriculum and the Frontiers in Biomedical Science course. Advanced Biochemistry courses and/or other graduate courses may be recommended by the student's Special Committee, depending on the student's background and interests.

Courses

Medical Biochemistry. This course is designed to provide the student with a knowledge of the fundamentals of biochemistry and an appreciation of the molecular basis of biological phenomena. There is an emphasis on the biochemical and molecular events relevant to human health and disease. The course is offered to both graduate and medical students. Topics covered include chemical and physical properties of biomolecules, enzymology, molecular biology, metabolism of carbohydrates, lipids, amino acids, purines, and pyrimidines. First and second quarters, annually. Dr. Tate.

Proteins: Structure and Molecular Properties. This course will cover the structure, folding and interactions of proteins with the emphasis on relating structure to biological function. Biophysical techniques will be introduced and their applications outlined. Third quarter, Structural Biology Staff.

Protein-Nucleic Acid Complexes: Structure and Function. This course will cover known structures of protein-DNA and protein-RNA complexes and their role in replication, transcription, translation and recombination of the genetic code. Fourth quarter, Dr. Patel.

Membrane Biochemistry. This course consists of a series of 15 lectures covering topics on structure-function relationships during membrane biogenesis and cell-cell interactions. Topics include membrane composition, membrane cell biology, physical techniques to study membrane structure, membrane receptors and stimulus-response coupling, membrane pathophysiology, thermodynamics, and the molecular aspects of membrane fluidity. These topics will be taught assuming that students have taken the first-year Core Curriculum Course. Fourth quarter. Dr. D. Hajjar.

Journal Club. This meets twice a month during the academic year and is required for all graduate students. Students and postdoctoral fellows meet, with faculty supervision, to discuss recent papers of biochemical importance. Student participation involves the presentation of papers and critical discussion of their contents and significance. Staff.

Other Academic Offerings

Introduction to Research. Laboratory rotations in experimental biochemistry dealing with the isolation, synthesis, and analysis of substances of biochemical importance (enzymes, proteins, nucleic acids, lipids, and metabolic intermediates), and study of their properties by various chemical and physical techniques. The student obtains this varied research experience by spending approximately two months in the laboratory of each of three faculty members of his or her choice. For incoming graduate students majoring in biochemistry and structural biology.

Biochemistry Seminars. A seminar series in which students, faculty, and invited scientists from this and other institutions report on progress in their laboratories.

Cell Biology and Genetics

Graduate Program Chairpersons

Joan Massagué, Sloan-Kettering Institute, Cell Biology & Genetics Program, 1275 York Avenue, New York, N.Y. 10021, (212) 639-8975

Enrique Rodriguez-Boulan, Department of Cell Biology & Anatomy, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6158

Graduate Program Director

David M. Bader, Department of Cell Biology & Anatomy, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-6149

The Program in Cell Biology and Genetics offers advanced study leading to the PhD degree. The program is intended to prepare students for a career in basic research and teaching in cell or developmental biology, genetics, molecular biology, or related disciplines.

Course Requirements: In the first two years students are expected to complete a core curriculum consisting of the core course Cell Structure and Formation, Advanced Cell Biology, and Molecular Genetics. First-year students also participate in a formal journal club designed to foster skills in literature comprehension and oral presentation. To satisfy the requirements for the PhD, the students also select four quarters (one year) of elective courses chosen to complement their background and develop their interests.

At the end of the first year, an oral evaluation of each student is conducted in order to monitor student progress and identify areas of strength and weakness. Students are also urged to participate in a weekly forum in which they and post-doctoral fellows report on their research, and are expected to attend one of the weekly research symposia hosted by the departments of Cell Biology & Anatomy or Cell Biology & Genetics. Although the official transcript reports only three grade levels, students are expected to perform at a level corresponding to a B average.

Laboratory Rotations: Students rotate through three laboratories during the first year. Such rotations familiarize students with ongoing research in the Program and provide a mechanism for selection of the thesis sponsor. Written rotation reports also provide practice in the skills of presenting scientific data.

Admission to Doctoral Candidacy: The Program administers a qualifying examination before the end of the second year of residence. The specific format of the examination, which is composed of written and oral sections, is determined by the examining committee. Typically, the written examination covers three or four topics selected by the student and committee, and the oral examination centers around a brief research proposal on a topic chosen by the student and not related to the thesis project.

Courses

Cell Structure and Function (see p. 73). All students in the Cell Biology and Genetics Program are required to take this two-quarter core course during their first year. The course covers basic information concerning biochemical, molecular, and physiological processes in cells. This will provide the foundation required for more specialized courses to suit the particular needs of each student.

Advanced Cell Biology. A series of month-long courses in selected topics in cell biology will be offered and will have 16–20 contact hours per course. These highly focused courses will present material on topics such as cell cycle regulation, cell motility, cell/cell and cell/matrix interactions, receptors and second message systems, protein sorting and additional areas of interest. Courses will run back to back so that students will be able to select topics of individual interest. A list of courses and faculty will be provided at the beginning of each academic year. Offered in the third and fourth quarters annually. Staff.

Molecular Genetics. The class focuses on key topics of molecular genetics in bacteria and bacterial viruses, yeast, nematodes, *Drosophila*, mouse, mammalian cells in culture and their viruses. Topics may include chromosome structure, transcriptional and translational regulation, genomic plasticity and elements of genetic diversity. The isolation of mutants and their analysis by recombination, complementation and the generation of suppressors are discussed in depth. The course consists of lectures and interactive small-group discussions of research papers from the current literature. Limited to 36 students. Offered as two sequential two-quarter courses, with the first half focusing on basic concepts, prokaryotic and simple eukaryotic systems, and the second half covering complex eukaryotic systems and special topics. Quarters I and II: Drs. Caudy, Chao, Holloman, Lustig, Osley, and Traktman. Quarters III and IV: Drs. Dorsett, Jasin, and Lacy.

Developmental Biology. Principles of descriptive, experimental, and molecular developmental biology are presented, using several animal systems as examples. Early development of the whole organism and of cells, tissues, and organs are considered. Prerequisites: consent of the faculty. Limited to 15 students. Offered in alternate years; third and fourth quarters in 1994–95. Drs. Bachvarova and Bader.

Practicum in Biological Optics. A workshop in practical aspects of light and electron microscopy. Following a weekly lecture, students conduct specific protocols involved in light and electron microscopy. Topics covered include: tissue fixation, embedding and thin sectioning; transmission and scanning electron microscopy; shadow-casting of proteins and nucleic acids; immunocytochemistry; fluorescence, phase and interference microscopy; laser-scanning confocal microscopy; image reconstruction; photography. All participants are required to complete an independent project. Prerequisite: consent of instructors. Course requirements include the completion of an independent project paper. Limited to 10 students. Offered in alternate years; third and fourth quarters in 1995–96. Ms. Cohen-Gould, Dr. Fischman, and staff.

Biophysics for Biologists. In this new course, concepts and methodological approaches in biophysics will be applied to current research problems in cell biology and physiology, emphasizing molecular structure and function. The course will be offered annually with alternating subject material. In 1995, the course will address the structure, dynamics and function of membrane lipids and proteins. Two combined lecture and research paper discussions per week. Fourth quarter, Drs. Andersen, Breslow, Pardee, Roepe, and Scotto.

Medical Genetics. This course covers aspects of human genetics in depth. The course will present lectures by the faculty and guest speakers on topics which explore the organization of the human genome, gene mapping and linkage, cytogenetics, genetic factors that contribute to normal human variation, inherited and *de novo* genetic alterations that lead to disease states, and application of genetic knowledge to clinical medicine. Dr. Chaganti and staff. Offered in alternate years; first and second quarters in 1995–96.

Journal Club Seminar for First-Year Students. This seminar is designed to give first-year students a chance to improve their skills in presenting and analyzing scientific data. Each student presents two papers during the semester. Papers are chosen by the students and approved by the instructors. Speakers generally provide a brief relevant background and then present each figure in the paper, summarizing the experimental method or assay used, the results illustrated, and the conclusions drawn. Participation by all students is encouraged during the presentation. Given jointly with the Molecular Biology program. Offered annually, third and fourth quarters. Drs. Blobel, Caudy, O'Donnell, Sheffery, and Shuman.

Graduate Student Seminar. This informal seminar is designed to improve graduate students' skills in public presentation. On a rotating basis, students prepare an oral presentation on their research or on a topic of their choice. The presentation is informally critiqued by the faculty. First through fourth quarters, annually.

Cell Biology and Microscopic Anatomy. Offered by the staff of the Program in Cell Biology and Genetics in conjunction with the Faculty of the Cornell University Medical College. This course follows a cellular and differentiative approach aimed at understanding the structure-function correlates that characterize the different tissues and organs. Lectures are complemented by small-group discussions and laboratory exercises designed to provide students with the skills to study and analyze cells and tissues. A microscope slide collection, presenting tissues and organs in a variety of physiological and developmental states, as well as correlative electron micrographs, are provided for individual study in the laboratory. Second and third quarters, annually. Drs. Bachvarova and Falcone.

Gross Anatomy. Regional anatomy is studied principally through dissection of the human body. Supplementing this technique are prosections by instructors, tutorial group discussions, and radiographic and endoscopic demonstrations. Enrollment is limited and students should consult the staff early in order to determine the availability of places. First and second quarters, annually, Drs. Hagamen and Weber, and the staff.

Thrombosis and Atherosclerosis. This course introduces graduate students to the topic of vascular cell biology from the clinical viewpoint of thrombosis and atherosclerosis. The course meets as a seminar for one hour per week for eight weeks. Each week students are asked to read 2–3 seminar papers from the recent literature. During the seminar, students and faculty engage in a round-table discussion of the papers, with emphasis on key hypotheses, experimental approaches, and future directions. Students are assigned to write an original paper in the form of a research grant at the completion of the course. Topics chosen in 1993–94 included the molecular basis of platelet activation, cell adhesion in vascular biology, endothelial cell activation, Herpes virus as a pathogenic agent in atherosclerosis, and the cell biology of lipoproteins. Minimum participation of two students is required. This course is offered annually and its schedule is arranged with interested students. Dr. Silverstein and staff.

Immunology

Graduate Program Chairpersons

Kenneth O. Lloyd, Sloan-Kettering Institute, Immunology Program, Kettering Laboratory, 1275 York Avenue, New York, NY 10021, (212) 639-2257

Kendall A. Smith, Department of Medicine, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, (212) 746-4464.

Graduate Program Director

Janet S. Lee, Sloan-Kettering Institute, Immunology Program, 1275 York Avenue, New York, NY 10021, (212) 639-8252

The program of study is developed for each student individually on the basis of the student's interest and prior experience. Immunology students generally take a core of formal courses offered by the graduate school in immunology, biochemistry, molecular biology, cell biology and genetics in order to complement their previous background and fulfill their own academic objectives. Participation in a graduate student seminar course is expected of all students to provide experience in oral presentation. Admission to Doctoral Candidacy at the end of the second year requires both written and oral examinations of the candidate's general understanding of immunology and related subjects which are relevant to the proposed research. However, the main focus of the graduate program in immunology is on laboratory research. Each student is required to undertake at least two minor research projects with different faculty members prior to developing a major research proposal for the doctoral thesis. This allows for laboratory experience to begin during the first year of the student's program. By the third year the doctoral candidate begins a full-time thesis project which typically takes two to three years. During this time the student will continue to participate in the other educational programs offered by the Institute. These include a wide variety of research seminars which are offered throughout the year with speakers from outside the Institute. In addition, the Immunology Program offers a series of colloquia on current topics in immunology with presentations and discussions led by Immunology faculty members.

Applicants should have a strong undergraduate background in the biological sciences, including biochemistry, molecular genetics and microbiology and are also expected to have some undergraduate laboratory research experience. The application requires a personal statement describing the student's background and specific interest in the Immunology Program. An official transcript of the student's undergraduate record is also necessary with at least two letters from faculty members who can evaluate the academic potential of the student in a PhD program in Immunology. Applicants must also submit the results of the Graduate Record Examination including the advanced test in Biology or Chemistry.

Courses

Current Topics in Immunology. This course during Quarters I and II provides a comprehensive overview of immunology beginning with the specific interactions of target cells and T cells that are regulated by the MHC molecule and peptide antigens on the target cell and the antigen specific T cell receptor. The development of antigen specific T cells in the thymus and their activation in the periphery, plus the development and activation of B cells are covered in detail. Specific roles for cytokines or lymphokines in the immune response are also important topics.

Quarters III and IV of the course cover the contribution of innate or antigen-nonspecific mechanisms of immunity. In addition, topics of clinical relevance such as allergy and autoimmunity, tumor immunology, congenital and acquired immunodeficiencies, transplantation immunology, and aging are discussed. The course is directed by Dr. Lee and the Immunology Faculty.

Cell Structure and Function (see p. 73). All students in the Immunology Program are required to take this two-quarter core course during their first year. The course covers basic information concerning biochemical, molecular, and physiological processes in cells. This will provide the foundation required for more specialized courses to suit the particular needs of each student.

Other Courses. Immunology students will be required to fulfill four quarters of electives in addition to the two courses described above. A list of possible courses is approved by the student evaluation committee each year, but includes: Molecular Genetics, Nucleic Acid Enzymology, Channels Pumps and Receptors, Molecular Biology of Cancer, and Introductory Pharmacology.

Graduate Research Seminar. This course is designed to provide all Immunology Program students with experience in preparing and giving oral presentations. Each student is required to give several talks based on various topics from their research and the current literature.

Molecular Biology

Graduate Program Chairpersons

Kenneth I. Berns, Department of Microbiology, Cornell University Medical College, Room B-308, 1300 York Avenue, New York, NY 10021, (212) 746-6505

Kenneth J. Marians, Molecular Biology Program, Sloan-Kettering Institute, Room 1101A, Rockefeller Research Laboratories, 430 E. 67th Street, New York, NY 10021, (212) 639-5890.

Graduate Program Director

Mary Ann Osley, Molecular Biology Program, Sloan-Kettering Institute, Rockefeller Research Laboratory, Room 901E, 1275 York Avenue, New York, NY 10021, (212) 639-7655.

The Graduate Program in Molecular Biology brings together faculty members from a number of different departments who share common scientific interests. These departments include the Program in Molecular Biology of the Sloan-Kettering Institute and the Departments of Microbiology and of Cell Biology and Anatomy of Cornell University Medical College. This extended faculty provides the student with a broad spectrum of research opportunities and advanced courses. The Graduate Program in Molecular Biology prepares students for a career in basic research by providing them with both a strong academic background in molecular biology, genetics, and cell biology, and training as an experimentalist through laboratory rotations and thesis research.

Admission: A good background in genetics, molecular biology, chemistry, or biochemistry is required of students. Graduate Record Examination scores in both the aptitude test and an advanced test (biology, chemistry, or biochemistry, cell and molecular biology) are also required.

Course Requirements: During their first year, students complete a core sequence of Cell Structure and Function (see p. 73), Graduate Biochemistry, Molecular Genetics, Eukaryotic Gene Structure and Function, and Journal Club Seminar. In addition, students participate in the Graduate Research Seminar Course throughout their enrollment. To complete the course requirements, six additional quarter-equivalents of elective coursework are taken before graduation, chosen from a list of courses approved by the Curriculum Committee. This list currently includes: Nucleic Acids Enzymology, Advanced Cell Biology, Developmental Biology, Molecular Genetics, Molecular Virology, Molecular Biology of Cancer, Practicum in Biological Optics, and Current Topics in Immunology.

All students, both PhD and MD-PhD, may petition the Curriculum Committee to exempt them from required or elective courses, if they can document taking equivalent courses at other undergraduate or graduate institutions.

Laboratory Rotations: Students are required to rotate through three laboratories. Laboratory rotations begin immediately after a series of lectures by the faculty designed to familiarize students with the research underway in their laboratories. It is expected that students will have chosen their thesis mentors by the start of their second year in the program.

Admission to Doctoral Candidacy: The Admission to Candidacy Examination (ACE) is administered in two sections: a written exam and an oral exam. For the written exam, the student prepares a written research proposal on a topic selected by the student and approved by the ACE committee. The written proposal is reviewed by the ACE committee and returned to the student with a written critique. The oral exam tests a student's ability to respond to the comments in the critique as well as a student's general knowledge in the field of the proposal. This examination is given either in the Spring of the second year or the Fall of the third year.

Special Committee: A student's Special Committee will be chosen by the student in consultation with his/her mentor when the student selects a laboratory for thesis research. The function of the Special Committee is to evaluate the direction and progress of a student's thesis research and to provide an informational resource to the student.

Curriculum Committee: This committee, chaired by the Program Director and consisting of 8–10 members of the faculty, oversees all educational aspects of the program. The committee is responsible for assembling the curriculum, setting course requirements, adjudicating student applications for exemption from course requirements, and administering the evaluation of students at the end of their first year.

Academic Requirements for Students in the MD-PhD Program: MD-PhD students enter the Graduate Program following completion of (1) the Frontiers in Biomedical Science course, (2) two laboratory rotations during the summers preceding the first and second years of medical school, and (3) the first two years of the medical school curriculum, including Biochemistry and quarter II of Cell Biology and Microscopic Anatomy. The academic requirements for MD-PhD students are designed to prepare them for competitive careers in biomedical research in the interrelated fields of molecular biology, cell biology, and genetics. MD-PhD students initiate their thesis research during their third year; during which they complete the core sequence of courses. The ACE is administered to MD-PhD students in the Fall of the fourth year. Starting in the Spring of their fourth year, they annually present a seminar on their thesis research in the Graduate Research Seminar Course.

Courses

Cell Structure and Function (see p. 73). All students in the Molecular Biology Program are required to take this two-quarter core course during their first year. The course covers basic information concerning biochemical, molecular, and physiological processes in cells. This will provide the foundation required for more specialized courses to suit the particular needs of each student.

Eukaryotic Gene Structure and Function. A quarter-long course presenting the fundamentals of eukaryote gene structure, expression and regulation. Topics discussed include: DNA sequence organization, chromatin structure, viral and cellular RNA transcription, translation and its regulation, control of gene expression in model systems and molecular aspects of carcinogenesis. Third or fourth quarter, annually. Dr. Freedman and staff.

Nucleic Acids Enzymology. A formal course presenting the enzymological mechanisms and control of prokaryotic and eukaryotic transcription and DNA replication. Enzymes which alter DNA structure and shape are reviewed, and topics in DNA repair and recombination are also covered. Graduate Biochemistry is a prerequisite. First and second quarters, alternate years. Offered in 1995–1996. Drs. Marians, Hurwitz, Holloman and O'Donnell.

Molecular Virology. A formal course in which major emphasis is placed on the basic mechanisms in the biology of all animal viruses, including RNA and DNA tumor viruses. The topics considered include virus structure and composition, assay of viruses and viral-specific products, transcription and replication of viral nucleic acids, translation of virus-specific proteins, assembly of viral particles, structural and functional alterations in viral-infected cells, including transformation, pathogenesis of viral diseases, and viral genetics. Alternate years. Offered third and fourth quarters, 1994–95. Drs. Besmer, Traktman, Lusky, and staff.

Molecular Genetics. This course, which is offered jointly with the Program in Cell Biology and Genetics, focuses on key topics of molecular genetics in bacteria and bacterial viruses, yeast, *Drosophila,* and mouse.The isolation of mutants and their analysis by recombination, complementation and the generation of suppressors are discussed in depth.The course consists of lectures and interactive small-group discussion of research papers from the current literature. Limited to 36 students. Offered in 1994–95 as two sequential two-quarter courses with the first focusing on prokaryotic and simple eukaryotic systems, and the second covering complex eukaryotic systems and special topics. Quarters I and II: Drs. Chao, Caudy, Holloman, Lustig, and Osley. Quarters III and IV: Drs. Dorsett, Jasin, and Lacy.

Molecular Biology of Cancer. This course focuses on current efforts to understand the neoplastic cell phenotype from a molecular point of view. The effects of RNA and DNA tumor viruses on host cells are discussed, in particular the transformation and/or differentiation blocks of defined cell lineages by certain agents.The nature and enzymatic specificities of viral gene products responsible for transformation are compared with related products of normal cellular genes. The potential interaction of such products with regulatory systems controlling cell shape, adhesiveness, motility, and mitosis are described, as well as the possible involvement of the same systems in nonviral neoplasias. A section of the course is devoted to the molecular biology and biochemistry of cell surface growth factor- and polypeptide hormone-receptors and mechanisms of signal transmission across biological membranes. At least part of the course consists of student presentations on relevant subjects.Third and fourth quarters, alternate years. Offered in 1995–96. Dr. Brown.

Graduate Research Seminar. This course represents an opportunity for all the faculty and students of the program to hear the upper-class students describe their research in formal seminar presentations. Quarters I–IV, annually. Dr. Lacy.

Journal Club Seminar for First-Year Students. In this seminar, first-year students present and analyze scientific data. Each student presents two papers during the semester. Papers are chosen by the students and approved by the instructors. Speakers generally provide a brief relevant background and then present each figure in the paper, summarizing the experimental method or assay used, the results illustrated, and the conclusions drawn. Participation by all students is encouraged during the presentation. Given jointly with the Program in Cell Biology and Genetics. Annually, quarters III and IV. Drs. Blobel, Caudy, O'Donnell, Sheffery, and Shuman.

Neuroscience

Graduate Program Chairman

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Graduate Program Directors

John A. Wagner, Department of Neurology and Neuroscience, Cornell University Medical College, Room E-615A, 1300 York Avenue, New York, NY 10021, (212) 746-6586

Gavril W. Pasternak, Department of Neurology, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10021, (212) 639-7046

The Program in Neuroscience provides training in the study of the nervous system. It includes the disciplines of neuroanatomy, developmental neurobiology, neurophysiology, molecular biology, neurochemistry, molecular genetics, neuropharmacology and neuropsychology. The program emphasizes a multidisciplinary approach based on the belief that future advances in our understanding of the nervous system will be derived from the strategies and research techniques employed by more than one discipline.The program of research and course work for entering students is individualized. Students are expected to spend time working closely with members of the faculty whose research approach is complementary to their interests. In addition, there are regularly scheduled seminars during which various aspects of work in process are presented and discussed. By these means, students are afforded the broadest possible view of the neurosciences during their graduate training.

Admission: Applicants to the program are expected to have had thorough undergraduate training in biology, organic chemistry, physics, and mathematics. Many students enter this program after attaining an MD or a masters degree, and this is taken into consideration in formulating their training program. Graduate Record Examination scores are to be submitted with the application. Candidates for admission are encouraged to visit the program.

Course Requirements for students in the PhD Program: Depending on prior background and needs, students will be expected to take a core sequence of courses during the first two years which includes introductory graduate courses in cell biology, molecular biology, and pharmacology, and Neuroscience Program courses in molecular, biochemical, cellular, and systems neurobiology. "Cell Structure and Function" (see p. 73) is an interdisciplinary course for first-year students that provides essential background for many entering students. Students will also select advanced graduate courses in the neurosciences and related fields to deepen their knowledge in areas of interest and develop a minor specialty. There is sufficient flexibility in choosing elective courses that students may specialize in a particular area(s), including molecular neurobiology, developmental neurobiology, systems neuroscience, neuropharmacology, or neurophysiology. Throughout their training, students are expected to participate in the weekly Progress in Neuroscience seminar series and the seminar companion course, Current Topics in Neurobiology.

Laboratory Rotations: These rotations allow students to experience research first-hand and to acquaint themselves with the research faculty of the Program. Students are expected to do two rotations of two quarters each but may do more rotations before choosing their respective thesis advisors.

Admission to Doctoral Candidacy: Before the end of the second year, students will organize a special committee and take the qualifying Admission to Doctoral Candidacy Examination. In the Neuroscience Program, this exam is a combination of a tutorial-style review of selected subjects that are of interest to the student, followed by a written exam and an oral defense of a research proposal.

Course Requirements for students in the MD-PhD Program: Students in the MD-PhD program will enter the research-intensive period of their training having completed both the first two years of the medical school curriculum and the Frontiers in Biomedical Science course. During the three years that these students spend in graduate studies, their major focus is laboratory research and preparation of research papers and a thesis, but students are also expected to participate in research-oriented seminars. To prepare them for their research career, students are expected to take a total of four, one-quarter graduate courses. Generally, students in the Program take the Admission to Doctoral Candidacy Examination at the end of their third year.

Courses

Cell Structure and Function in the Nervous System. This course is coordinated with the interdisciplinary "Cell Structure and Function" course, and presents related concepts that are fundamental to understanding the nervous system. Topics covered include: regulation of gene expression in neurons and glial cells, control of neurotransmitter synthesis, the biology of the synapse, signal transduction by cell surface receptors, polarization of neurons, axonal transport, membrane potential and neurophysiology. The course will emphasize the molecular, cellular, and biochemical research opportunities in the nervous system. First and second quarters, annually. Co-registration in "Cell Structure and Function" is usual. Dr. Duvoisin and faculty of the Program in Neuroscience.

Developmental Neurobiology. This course will explore fundamental concepts in the development and maintenance of the nervous system. Major topics include classical neuroembryology, inductive effects, cell lineage, determination of cell fate, axonal guidance, synaptogenesis and specificity of synapse formation, cell-cell interaction, and naturally occurring cell death. Third quarter, annually, Dr. Pickel and faculty of the Program in Neuroscience.

Neuropharmacology and Functional Neuroanatomy. This course is jointly sponsored by the Program in Neuroscience and the Program in Pharmacology. It is designed to present current concepts of the

major central nervous system (CNS) neurotransmitters and their functional neuroanatomy. The course will integrate discussions of the mechanisms of neurotransmitter biosynthesis and release, receptor signal transduction and the alterations produced by CNS drugs, with a description of how contemporary neuroanatomical methods are used to define neurotransmitter systems, their functions, and their interactions with drugs. Offered third and fourth quarters, annually. The course includes laboratory sessions. Course organizers: Drs. Inturrisi, Milner, and Okamoto. Co-Instructors: Drs. VanBrockstaele and Aicher.

Integrative Neuroscience and Experimental Design. This is an interdisciplinary course on the structure and function of the human nervous system given jointly by the Department of Physiology and Biophysics and the Department of Cell Biology and Anatomy, with the participation of the Department of Neurology and Neuroscience. It includes lectures that correlate anatomical, physiological, and clinical aspects of neuroscience. It includes computer-based teaching mules on neuroanatomy and neurophysiology, patient presentations, and discussions of current experimental problems. It draws a substantial amount of material from the Medical Neuroscience course co-organized by Drs. Brooks and Grafstein. Offered fourth quarter annually by Drs. Ruggiero and Stensaas, and faculty of the Program with the assistance of Dr. Brooks.

Molecular Basis of Neurological Disease. This course will review current attempts to understand neurological disease from a molecular and pathophysiological point of view. Students will be taught the background basic methods in molecular biology, molecular genetics and pathology. They will learn how to apply these to study a variety of neurological disorders chosen on the basis of their importance to human disease and on the basis of interesting experimental approaches that can be exploited at the molecular level. Topics will include muscular dystrophy, myotonic dystrophy, myasthenia gravis, Alzheimer's disease, Huntington's disease, stroke, multiple sclerosis, Charcot-Marie-Tooth disease, Parkinson's disease, fragile X syndrome, multiple sclerosis and selected psychiatric disorders. The course will consist of both lectures and informal discussions of recent research papers. The exam will include the development of an original research proposal. First and second quarter, annually. Drs. Furneaux and Reis, and faculty of the Program.

Channels Pumps and Receptors. See description under Physiology and Biophysics. First quarter, annually, Dr. Maack.

Molecular and Cellular Electrophysiology. This course is offered jointly with Physiology and Biophysics and a description is provided under their listing. Second quarter, annually, Drs. Andersen, Gardner, Palmer, and staff.

The Visual System. Lectures and readings on the functional organization of the vertebrate visual system at the molecular, cellular and systems levels. Topics will include phototransduction and signal processing within the retina, lateral geniculate nucleus and visual cortex. Second and third quarters, annually, Drs. MacLeish and Victor.

Mathematical Methods in Neuroscience. The aim of this course is to provide a didactic introduction to a variety of mathematical approaches in neuroscience, selected both because of their proven usefulness and their intrinsic interest. Mathematical structures traditionally considered "advanced" will be introduced in an elementary fashion. Applications to be considered will include the analysis of channel activity, the analysis of spike trains, and image analysis. First quarter, 1994-95, with adequate enrollment. Dr. Victor.

Cognitive and Behavioral Neuroscience. This course is concerned with the neural mechanisms of behavior. Current knowledge concerning the experimental analysis of a range of behaviors including memory, attention, language, emotion, and visual cognition in humans and animals will be presented and discussed. The reciprocal interactions between brain and behavior will be emphasized. In addition to attending the lectures and participating in discussions, each student will be required to write a concise and critical review of a topic in Behavioral Neuroscience. Second quarter, annually. Drs. Purpura and Silbersweig.

Functional Imaging of the Human Brain. Current developments in imaging technology (magnetic resonance imaging, MRI, and positron-emission tomography, PET) open a new window of opportunity for

neuroscientists to observe localized neural activity and to study neural organization in the human brain. The aim of this course is to introduce the fundamental principles of functional imaging (with a particular emphasis on MRI and PET) and to survey the literature and emerging new developments in Neurobiology. Students will have an opportunity to observe and participate in ongoing functional MRI investigations. Third quarter, annually. Dr. Hirsch.

Proseminar in Synaptic Physiology. See Course Offerings for Program in Physiology and Biophysics for description. Fourth quarter, with adequate enrollment.

Progress in Neuroscience. This course is the seminar series in the Program in Neuroscience. Most lectures are given by speakers invited from outside the Cornell community, but speakers are also drawn from the Program in Neuroscience and scientists at Cornell with related interests. Every quarter, annually, Drs. Grafstein, Wagner, and the seminar committee.

Progress in Neuroscience/Current Topics in Neurobiology. This course combines the seminar series in the Program in Neuroscience with critical discussions of papers published by the speaker, or related papers in the area of that week's seminar. Second and third quarters, annually. Dr. Gandy.

Pharmacology

Graduate Program Chairpersons

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Lorraine J. Gudas, Department of Pharmacology, Cornell University Medical College, Room E-409, 1300 York Ave., New York, NY 10021, (212) 746-6250

Graduate Program Director

Charles E. Inturrisi, Department of Pharmacology, Cornell University Medical College, Room LC-524, 1300 York Ave., New York, NY 10021, (212) 746-6235

The Program in Pharmacology brings together faculty members from the Department of Pharmacology, Cornell University Medical College and the Program of Molecular Pharmacology and Therapeutics of the Sloan-Kettering Institute for Cancer Research. This interdisciplinary faculty provides the student with a broad spectrum of research opportunities and advanced courses in pharmacology.

Admission: A baccalaureate degree with a strong background in the natural sciences and/or health sciences is required for admission. Results of the Graduate Record Examination (verbal, quantitative and analytical) are required for PhD applicants, while the results of the advanced test in Biology or Chemistry will be considered. For applications to the MD-PhD program, the results of the Medical College Admission Test are accepted in lieu of the Graduate Record Examination.

Course Requirements: In the first two years, students complete a core curriculum that includes the following courses: Introduction to Pharmacological Principles, Cell Structure and Function, Biostatistics, Physiology and Biophysics, General Pharmacology, Molecular Pharmacology, Neuropharmacology and Functional Neuroanatomy and Pharmacology Research Seminars. The Cell Structure and Function course is required in each of the graduate programs. Each student also completes two electives by June of the second year. These electives are selected from courses that are offered by other programs at the graduate school. Recent choices include: Graduate Biochemistry, Advanced Cell Biology, Channels, Pumps, and Receptors, Current Topics in Immunology, Neuroscience, and Molecular Mechanisms of Disease.

Program Supervision and Laboratory Rotations: The Program Director and the Curriculum Committee will supervise the student's graduate program until the student selects a faculty member to serve as the major sponsor. Three laboratory rotations are required of each student. These rotations provide the opportunity for the student to participate in the diverse research activities that are available within the Program. This experience is designed to assist the student in the selection of major and minor sponsors for the thesis research.

Admission to Doctoral Candidacy: The Admission to Candidacy Examination consists of two parts: a uniform written exam and an oral exam which includes discussion of a written research proposal. It is expected that most students will take this exam by the end of May of their second year.

Special Committee: The Special Committee is comprised of a major faculty sponsor and two minor faculty sponsors. The Program Director will assist the student in the selection of the major (thesis) advisor.

Retreat: The Pharmacology Program holds a retreat each year in the spring, usually for two days at a country inn. Members of the Program gather for a series of informal talks and a poster session to exchange the latest scientific information. This provides a relaxed setting for new, incoming graduate students to meet other graduate students, postdoctoral fellows, and faculty members in the department.

Courses

Introduction to Pharmacological Principles. This course is designed to introduce the student to concepts fundamental to pharmacology including receptor theory, the dose-response relationship, mechanisms of drug action and resistance, pharmacokinetics, metabolism, tolerance and dependence. These topics are intended to complement and extend areas covered in the concurrently offered core course entitled Cell Structure and Function (see Course Requirements). All first-year graduate students in pharmacology are required to take this course, which is also open to all students in the graduate school. First and second quarters, annually. Drs. Gross and Prochaska.

General Pharmacology. This basic pharmacology course consists of lectures, demonstrations, and small-group conferences. The purpose of these exercises is to teach the principles of pharmacology to second-year medical students and to graduate students. Detailed consideration is given to the parameters of drug action to provide the student with the fundamental concepts essential for evaluation of any drug. Consequently, the scientific basis of pharmacology is emphasized. Prototype drugs, essentially considered systemically, serve to illustrate several mechanisms and parameters of drug action. Therapeutic applications are considered insofar as they illustrate principles of pharmacology or drug hazards. This course is required for all pharmacology students in their second year. Second and third quarters, annually. Dr. Chan and staff.

Neuropharmacology and Functional Neuroanatomy. This course is jointly sponsored by the Programs in Neuroscience and Pharmacology. It is designed to present current concepts of the major Central Nervous System (CNS) neurotransmitters and their functional neuroanatomy. The course will integrate discussions of the mechanisms of neurotransmitter biosynthesis and release, receptor signal transduction and the alterations produced by CNS drugs, with a description of how contemporary neuroanatomical methods are used to define neurotransmitter systems, their functions and interactions with drugs. The course includes laboratory sessions. Offered annually third and fourth quarters. Course organizers: Drs. Milner, Inturrisi and Okamoto. Co-Instructors: Drs. Van Bockstaele and Aicher.

Molecular Pharmacology of Cancer. This course examines drug action at the molecular level, particularly with respect to cancer therapeutics and consists of both lectures and reviews of current journal articles. Topics include mechanisms of drug resistance, oncogenes and tumor suppressor genes, computer based drug design, immunotherapy, hormone therapy, differentiation agents, tumor promotion and environmental toxins, tumor angiogenesis, tumor metastasis. Offered 1994-95, fourth quarter. Drs. Bertino, Scotto, and staff.

Pharmacology Research Seminars. Topics of contemporary pharmacological interest and new concepts and methodological approaches in biological research will be presented by guest speakers, faculty members or students. The presentations are followed by a discussion session which provides an opportunity for students to meet and talk to leading scientists in the field. Details of events will be announced in advance. Annually, third and fourth quarters. Drs. Buck, Roepe, and Szeto.

Other Academic Offerings

Research in Pharmacology. Research opportunities may be arranged throughout the year for graduate students who are not majoring in pharmacology but who want some investigative experience in the discipline. Special opportunities are offered for work on the nervous and cardiovascular systems and in biochemical and clinical aspects of pharmacology.

Journal Club. This course is designed to improve graduate students' skills in public presentation. On a rotating basis, students prepare an oral presentation on a topic of their choice. The presentation is informally critiqued by the faculty. First through fourth quarters, annually; see the Program Director for further information.

Physiology and Biophysics

Graduate Program Chairman

Erich E. Windhager, Department of Physiology and Biophysics, Cornell University Medical College, Room C-508, 1300 York Avenue, New York, NY 10021, (212) 746-6358

Graduate Program Director

Olaf S. Andersen, Department of Physiology and Biophysics, Cornell University Medical College, Room LC-501, 1300 York Avenue, New York, NY 10021, (212) 746-6350

Opportunities are offered toward the PhD degree in several areas of physiology and biophysics. Ample research space is available, and laboratories are well equipped to provide predoctoral training in a biomedical sciences. Interested individuals are urged to contact the Program Director before preparing a formal application. Letters of inquiry should include a discussion of the educational background and indicate possible areas of emphasis in graduate study. There has been a tendency to encourage applications from individuals who have a probable interest in more than one of the areas of physiology represented within the program.

Applicants must have completed admission courses in biology, inorganic and organic chemistry, physics, and mathematics through the level of differential and integral calculus. Additional course work in these disciplines at the undergraduate level is encouraged. The Graduate Record Examination is required and advanced subject tests are recommended. Applicants from abroad are, in addition, required to take the TOEFL examination. Applicants with otherwise exemplary records who lack certain course requirements will be considered for acceptance provided that they remedy their deficiencies while in training.

Course Requirements: The course of study emphasizes the importance of teaching and research in the preparation and development of individuals for careers in physiology. This goal is achieved by a combination of didactic courses, seminars, and closely supervised research leading toward the preparation of a satisfactory thesis.

A special program of study will be developed for each student in consultation with his or her Special Committee. For MD-PhD students the program will take into consideration their coursework during the first two medical school years. Students that enter with a MD or a master's degree will likewise have specially designed programs.

In the first two years, students are expected to satisfactorily complete a core curriculum that will be tailored to fit the professional needs of each student. The curriculum will be determined by the student's previous coursework and likely research area. The core curriculum usually will include:

1. Courses in Physiology and Biophysics:
   The graduate course in Channels, Pumps, and Receptors.
   The general course in Physiology and Biophysics (including endocrinology) for medical and graduate students.
   The general course in Neuroscience for medical and graduate students.
   At least one of the advanced graduate courses/seminars offered by the field.
2. Biochemistry:
   The core course on Cell Structure and Function (see p. 73)
   In addition most students should take an advanced Biochemistry course.
3. Cell Biology:
   The graduate course in Advanced Cell Biology.
4. Molecular Biology and Genetics:
   Depending on the student's research interests, one or more courses chosen by the student in consultation with his/her advisor.
5. Pharmacology:
   The general course in Pharmacology for medical and graduate students.

In addition, all students must complete at least one laboratory rotation in addition to that of the Major Sponsor.

A thesis advisor will be chosen early in the second year, and a Special committee consisting of this major research advisor and two minor advisors will be constituted to guide the student in their research preparation. Students start their thesis research before completing their formal coursework,

but they re not admitted to PhD candidacy before passing the Admission to Doctoral Candidacy Examination towards the end of the second year or early in the third year.

Courses

Physiology and Biophysics. Lectures and conferences on body fluid, bioelectric phenomena, endocrinology and the cardiovascular system. Third quarter, 1994-95. Dr. Windhager and staff.

Endocrinology is taught as an interdisciplinary course during two weeks of the third quarter using hours normally allocated not only to courses in physiology, but also in cell biology, and biochemistry. Dr. Greif and staff.

Lectures and conferences on respiration, kidney function, acid-base regulation, and gastrointestinal function; and a weekly laboratory on selected aspects of physiology. Fourth quarter, 1994-95. Dr. Windhager and staff.

Integrative Neuroscience and Experimental Design. An interdisciplinary course on the structure and function of the human nervous system given jointly by the Department of Physiology and Biophysics and the Department of Cell Biology and Anatomy, with the participation of the Department of Neurology and Neuroscience. Includes lectures that correlate anatomical, physiological and clinical aspects of neuroscience, and computer-based teaching modules on neuroanatomy and neurophysiology, as well as patient presentations. Fourth quarter annually. Drs. Grafstein, Brooks and staff.

Channels, Pumps, and Receptors. This is an introductory course that describes the molecular basis for the function of biological membranes. Topics to be covered include: the structure and properties of biological membranes and membrane proteins; the molecular basis for receptor specificity, turnover, and intracellular signaling; the major classes of ion channels, their molecular and functional characteristics, and their modulation; and the structure and mechanism of ion pumps. The course will consist of lectures, conferences, and laboratory demonstrations. First quarter, 1994-95. Dr. Maack and staff.

Molecular and Cellular Electrophysiology. This course examines the electrophysiological properties of channels, cells, and simple systems. The aim of the course is to integrate the electrophysiology of single molecules with that of isolated cells and assemblies of cells, with emphasis on nerve, muscle, and epithelia. The course in Channels, Pumps, and Receptors is a prerequisite. Topics to be covered include: the genesis of resting membrane potentials and action potentials; synaptic transmission and neuronal integration; epithelial ion transport; sensory transduction; and modulation of electrical activity. Second quarter, 1994-95. Drs. Andersen, Gardner, Palmer, and staff.

Topics in Membrane Physiology and Ionic Channels. This is a weekly two-hour conference that addresses physiological problems from a more quantitative point of view. The aim is to train students in physiological concepts, in particularly the mathematical and experimental approaches relating to ion channels. The course will consist of lectures, demonstrations, and student presentations of selected papers. Third quarter, 1994-95. Dr. Andersen.

Mathematical Models of Membrane Transport. The general, thermodynamic description of membrane and epithelial transport will be reviewed (with reference to Katchalsky, Curran and Schultz, Sauer, Essig and Caplan). Comparison with kinetic descriptions of membrane transport will be considered (Heinz, Hill). The analysis of composite membrane systems will be examined (Kedem and Katchalsky) as a prelude to the construction of epithelial simulations (Sackin and Boulpaep, Weinstein and Stephenson). Examples of such simulations will be used to examine transport along the kidney tubule under normal and pathological conditions. Third and fourth quarter, 1994-95. Dr. Weinstein.

Selected Topics in Kidney and Electrolyte Physiology and Pathophysiology. Lectures, seminars and demonstrations. Topics include: (1) GFR, clearance concept, reabsorption and secretion of electrolytes; (2) concentrating mechanism; (3) electrophysiology of the nephron; (4) pathophysiology of potassium; (5) renal hemodynamics; (6) control of body fluid volume and tonicity; (7) control of acid base balance; (8) pathology and pathophysiology of renal failure. Minimum of 8 students. Fourth quarter, annually. Drs. Maack, Windhager, and staff.

Topics in Gastrointestinal Physiology. Lectures and Seminars. Topics include: (1) functional morphology of stomach and intestine; (2) proliferation and differentiation of gastrointestinal cells; (3) motility of esophagus, small intestine and colon; (4) gastric and intestinal secretion; pancreatic secretion; (5) lipid absorption; (6) intestinal absorption of calcium and vitamin D; (7) structure and function of bile acids; (8) gastrointestinal hormones. Minimum: 8 students. Fourth quarter, 1994–95. Dr. Lipkin and invited experts in the field.

Proseminar in Synaptic Physiology. The biophysics of synapses and their relation to behavior are explored by reading and discussion of seminal papers in the original literature. The first half of the course examines a model synapse, the mammalian neuromuscular junction, by intracellular recording, voltage clamping, noise analysis, and patch clamping. Topics in the second half include NMDA receptors, plasticity, and neural networks. Fourth quarter, 1994–95. Dr. Gardner.

Interdisciplinary Program in Molecular and Cellular Biology

Graduate Program Chairperson

Donald A. Fischman, Department of Cell Biology and Anatomy, Cornell University Medical College, Room A-112, 1300 York Ave., New York, NY 10021, (212) 746-4150

Successful applicants to the Interdisciplinary Program in Molecular and Cellular Biology are admitted "at large," i.e., without initial commitment to one of the seven more specialized PhD programs of the Graduate School of Medical Sciences. Students in the program participate in a core curriculum of courses and laboratory rotations which expose them to the many research opportunities at Cornell University Medical College and the Sloan-Kettering Institute. These activities eventually lead to the selection by the student of the laboratory of a participating faculty member for thesis research and to the student's affiliation with one of the more specialized PhD programs.

Application: A good background in the natural and physical sciences, including genetics, molecular biology, and chemistry or biochemistry, is required. The Graduate Record Examination (GRE) General Test and the Subject Test in chemistry, biochemistry, or cell and molecular biology are required.

First-Year Program:

Required courses and activities include:

1. Cell Structure and Function, a core course for all first-year students (see p. 73)
2. Molecular Genetics
3. Eukaryotic Gene Structure and Function
4. Advanced Cell Biology
5. Three laboratory rotations, to be completed by September of the second year

Elective courses:

1. Journal Club Seminar for First-Year Students
2. Graduate Student Seminar

Second-Year Program:

1. Selection of major sponsor, formation of Special Committee, and beginning of thesis-related research
2. Enrollment in elective courses offered by the seven programs of the Graduate School of Medical Sciences. Typical offerings include: Nucleic Acids Enzymology; Molecular Virology; Cell Structure and Function in the Nervous System; Developmental Biology; Current Topics in Immunology; Molecular Pharmacology of Cancer; Medical Genetics; Proteins: Structure and Molecular Properties; Channels, Pumps and Receptors
3. Admission to Doctoral Candidacy Examination

MD-PhD Program

Requirements for the PhD component of the MD-PhD Program are satisfied by completion of the first two years of the Medical College curriculum including the *Frontiers of Biomedical Science* course and 1 to 3 additional courses to be determined by the student's chosen Program of Study, with consideration of the prior experience of the student. During the first two summers the student is expected to complete laboratory rotation requirements. The tutorial-based Admission-to-Doctoral-Candidacy Examination will assist the student in developing a research thesis project.

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Stephenson, John L., Professor of Biomathematics in Physiology and Biophysics. B.A. 1943, Harvard University; M.D. 1949, University of Illinois

Stoeckle, Mark Young, Assistant Professor of Medicine. Assistant Professor of Medicine in Microbiology. A.B. 1974, Harvard College; M.A., M.D. 1978, Harvard Medical School

Stokes, Peter E., Professor of Medicine, Professor of Psychiatry. B.S. 1948, Trinity College; M.D. 1952, Cornell University Medical College

Stutman, Osias, Professor of Immunology. B.A. 1950, Colegio Nacional Sarmiento (Argentina); M.D. 1957, Buenos Aires University Medical School (Argentina)

Sussdorf, Dieter H., Associate Dean, Associate Professor of Microbiology. B.A. 1952, University of Missouri; Ph.D. 1956, University of Chicago

Szeto, Hazel H., Professor of Pharmacology. B.S. 1972, Indiana University; M.D. 1977, Cornell University Medical College; Ph.D. 1977, Cornell University Graduate School of Medical Sciences

Tate, Suresh S., Associate Professor of Biochemistry. B.Sc. 1958, M.Sc. 1960, University of Baroda (India); Ph.D. 1963, University of London (United Kingdom)

Tempst, Paul, Associate Professor of Molecular Biology and of Biochemistry and Structural Biology. B.S. 1976, Ghent State University (Belgium); Ph.D. 1981, Ghent University (Belgium)

Toth, Miklos, Assistant Professor of Pharmacology. M.D. 1977, Albert Szent-Gyorgyi Medical University (Hungary); Ph.D. 1985, Academy of Sciences (Hungary)

Townes-Anderson, Ellen, Adjunct Associate Professor of Physiology and Biophysics. Associate Professor of Physiology in Ophthalmology. B.A. 1968, Connecticut College; M.A. 1971, University of California, Berkeley; Ph.D. 1980, Boston University School of Medicine

Traktman, Paula, Associate Professor of Cell Biology and Anatomy. Associate Professor of Cell Biology and Anatomy in Microbiology. A.B. 1974, Radcliffe College, Harvard University; Ph.D. 1981, Massachusetts Institute of Technology

Udenfriend, Sidney, Adjunct Professor of Biochemistry. B.S. 1939, City College of the City University of New York; M.S. 1942, Ph.D. 1948, New York University

Victor, Jonathan D., Professor of Neurology and Neuroscience. B.A. 1973, Harvard University; Ph.D. 1979, The Rockefeller University; M.D. 1980, Cornell University Medical College

Volpe, Bruce T., Associate Professor of Neurology and Neuroscience. B.S. 1969, Yale College; M.D. 1973, Yale University School of Medicine

Wagner, John Anthony, Professor of Neurology and Neuroscience. Professor of Cell Biology and Anatomy. B.S. 1970, Loras College; Ph.D. 1975, Princeton University

Watanabe, Kyoichi A., Professor of Molecular Pharmacology and Therapeutics. Ph.D. 1963, Hokkaido University (Japan)

Weinstein, Alan M., Associate Professor of Physiology and Biophysics. Associate Professor of Medicine. A.B. 1971, Princeton University; M.D. 1975, Harvard University

Weksler, Marc E., The Irving Sherwood Wright Professor of Geriatrics in Medicine. B.A. 1958, Swarthmore College; M.D. 1962, Columbia University

Wellner, Daniel, Associate Professor of Biochemistry. A.B. 1956, Harvard University; Ph.D. 1961, Tufts University

White, Perrin C., Associate Professor of Pediatrics. A.B. 1972, Harvard University; M.D. 1976, Harvard Medical School

Wiedmann, Martin, Assistant Professor of Cell Biology and Genetics. Diplom 1975, University of Greifswald (Germany); Ph.D. 1979, University of Potsdam (Germany)

Windhager, Erich E., The Maxwell M. Upson Professor of Physiology and Biophysics. M.D. 1954, University of Vienna (Austria)

Yang, Soo Young, Associate Professor of Immunology. M.S. 1972, Minnesota State University; Ph.D. 1981, New York University

Zakim, David, The Vincent Astor Distinguished Professor of Medicine. B.A. 1956, Cornell University; M.D. 1961, State University of New York Downstate Medical Center

Zelenetz, Andrew, Assistant Professor of Medicine, Assistant Professor of Molecular Biology. A.B. 1977, Harvard University; M.D., Ph.D. 1984, Harvard Medical School

Degree Recipients 1993–94

Doctors of Philosophy

August, Avery, B.A. 1987, University of California at Los Angeles. Immunology, Professor Bo Dupont. Thesis: "On the Molecular Basis for the Two Signal Hypothesis of T-Cell Activation: Signalling by CD3 and CD28."

Bannerji, Rajat, B.A. 1986, Cornell University; Molecular Biology, Professor Eli Gilboa. Thesis: "Mechanism of Immune Response Induced by Cytokine Gene Modified Tumor Cells."

Blum, Michele DeCarlo, B.A. 1986, Lafayette College. Molecular Biology, Professor Elizabeth Lacy. Thesis: "Regulation of Human CD4 Gene Expression in Transgenic Mice."

Bosenberg, Marcus, B.A. 1976, Cornell University; Cell Biology and Genetics, Professor Joan Massagué. Thesis: "Regulated Release of Membrane-anchored Transforming Growth Factor-α."

Bradley, Roger, B.A. 1984, Carroll College; Cell Biology and Genetics, Professor Anthony Brown. Thesis: "Identification of Secreted Wnt-1 Protein and Analysis of its Mechanism of Action."

Cupp-Burris, Judith, B.S., B.A. 1987, Missouri Southern State College. Immunology, Professor Ulrich Hämmerling. Thesis: "The Role of Vitamin A in Normal B cell Activation."

Elliott, Robert, A.B. 1983, University of California. Neuroscience, Professor Ira Black. Thesis: "The Potential Role of Neurotrophic Mechanisms in Activity-induced Changes in Neural Function."

Fuortes, Michele, M.D. 1979, University of Rome. Cell Biology and Genetics, Professor Carl Nathan. Thesis: "Tumor Necrosis Factor and Cell Adhesion: Joint Control of Neutrophil Activation."

Glickstein, Lisa, B.S. 1987, Cornell University; Immunology, Professor Osias Stutman. Thesis: "Post-thymic T-cells: Thymus-independent Homeostasis and Evidence for Pluripotent Effector Function."

Grün, Felix, B.A. 1987, Girton College, Cambridge University (United Kingdom); Immunology, Professor Ulrich Hämmerling. Thesis: "The Physiology and Biochemistry of the Retro-retinoid, Anhydroretinol. From *Drosophila* to Man."

Hong, Guangyuan, B.S. 1982, M.S. 1985, Peking University. Molecular Biology, Professor Kenneth Berns. Thesis: "Studies on the Rescue and Replication of the AAV Genome *in vitro*."

Hsu, Katharine, B.S., M.S. 1987, Stanford University, Cell Biology and Genetics, Professor Moses Chao. Thesis: "Mechanisms of TNF Receptor Action: Studies Using Chimeric Receptor Mutants."

Huber, Louise Julie, B.S. 1985, Boston University, Cell Biology and Genetics, Professor Moses Chao. Thesis: "*In vivo* Regulation and Function of the p75 Neurotrophin Receptor."

Huh, Sungoh, B.S. 1984, M.S. 1987, Seoul National University (Korea), Neuroscience, Professor Tong H. Joh. Thesis: "Studies on the Regulation of Tryptophan Hydroxylase Gene Expression in the Serotonergic Cell Types of Transgenic Mice."

Leonard, Christopher J., B.S. 1985, Cornell University. Microbiology, Immunology, and Pathology, Professor Kenneth Berns. Thesis: "The Cloning, Expression and Partial Purification of Rep 78: A Replication Protein of Adeno-associated Virus."

Luo, Yan, M.D. 1987, Beijing Medical University. Molecular Biology, Professor Stewart Shuman. Thesis: "Mechanistic Study on Termination in Vaccinia Early Transcription."

Maddux, Regina Buck, B.A. 1988, Hunter College, Immunology, Professor Peter Besmer. Thesis: "W-sash Affects Positive and Negative Elements Controlling C-kit Expression: Ectopic C-kit Expression at Sites of Kit Ligand Expression Affects Melanogenesis."

Mahmood, Umar, B.S. 1987, California Insitute of Technology. Physiology and Biophysics, Professor Jason A. Koutcher. Thesis: "*In Vivo* and *In Vitro* Changes in ^{31}P Nuclear Magnetic Resonance Spectra Post Radiation."

Moran, Lorraine Macellaro, A.B. 1982, Mount Holyoke College; M.S. 1984, St. John's University. Molecular Biology, Professor Mary Ann Osley. Thesis: "Factors Involved in Temporal and Autogenous Control of Histone Synthesis in *Saccharomyces cerevisiae*."

Naftzger, Clarissa Cartier, B.A. 1985, University of California at Berkeley. Immunology, Professor Alan Houghton. Thesis: "Melanosomal Glycoproteins as Autoantigens: Generation of Antibodies Against Murine gp^{75}."

Prescott, John, B.S. 1985, Cornell University. Molecular Biology, Professor Erik Falck-Pedersen. Thesis: "Regulation of Poly (A) Site use in the Adenovirus Major Late Transcription Unit."

Rubin, Lisa Steiner, B.S. 1985, Cornell University, Pharmacology, Professor Roberto Levi. Thesis: "Pharmacological and Biochemical Evaluation of Kinin Involvement in Cardiac Anaphylaxis in the Guinea Pig Heart."

Spector, Mona Sue, B.S. 1980, Brooklyn College. Molecular Biology, Professor Mary Ann Osley. Thesis: Genetic Analysis of Positive and Negative Regulators of Histone Gene Transcription in *Saccharomyces cerevisiae*."

Stukenberg, Peter Todd, B.S. 1986, Colgate University, Molecular Biology, Professor Michael O'Donnell. Thesis: "The Dynamics of *E. Coli* DNA Polymerase III Holoenzyme in an *In Vitro* Lagging Strand Model System."

Masters of Science

Ghosh, Rita, B.S. 1977, M.S. 1980, Delhi University. Molecular Biology, Professor Paula Traktman. Thesis: "Overexpression, Purification and Biochemical Analysis of D5: A Protein Essential in Vaccinia DNA Replication."

Rao, Prakash, B.A. 1991, University of California at Santa Barbara. Cell Biology and Genetics, Professor Moses V. Chao. Thesis: "Mechanism of p^{75} Tumor Necrosis Factor Receptor Signaling."

Students 1994-95

Candidates for the Degree of Doctor of Philosophy

Entering Students

Akkihal, Anup Roop (Physiology and Biophysics). B.A. 1993, Johns Hopkins University. Huntington, West Virginia

Andejelkovic, Jelena (Biochemistry and Structural Biology). B.S. 1992, University of Belgrade, (Yugoslavia). Belgrade, Yugoslavia

Appleby, Susan Blixt (Molecular and Cellular Biology). B.S. 1988, Rochester Institute of Technology. Albany, New York

Babej, Sarah Thayer (Neuroscience). B.A. 1985, Earlham College; M.S. 1987, Georgetown University; M.D. 1991, University of Virginia School of Medicine. Tokyo, Japan

Bence, Kendra Kathleen (Physiology and Biophysics). B.A. 1993, Colgate University. Ithaca, New York

Cai, Hui (Cell Biology and Genetics). B.S. 1990, Sichuan University, (People's Republic of China). Fuzhou, People's Republic of China

Castella, Paul Charles (Cell Biology and Genetics). B.S. 1987, University of London, (England). London, England

Chen, Lian (Pharmacology). B.S. 1994, Ohio State University. Zuzhou, People's Republic of China

Choe, Han Seok (Physiology and Biophysics). B.S. 1989, Seoul National University, (Korea). Seoul, Korea

Crowe, Rebecca Lynn (Cell Biology and Genetics). B.S. 1994, Trenton State College. Hackensack, New Jersey

Davis, Antonia (Neuroscience). B.A. 1994, University of Pennsylvania. Salem, Massachusetts

Dimova, Dessislava Kostadinova (Molecular Biology). M.Sc. 1991, Sofia University, (Bulgaria). Sofia, Bulgaria

Fukuda, Seiya (Neuroscience). B.S. 1994, California Institute of Technology. East Patchogue, New York

Gibson, Eric (Pharmacology). B.S. 1988, Syracuse University. Monrovia, Liberia

Gilbert, Mathew Timmerman (Physiology and Biophysics). B.A. 1990, Oberlin College. Ithaca, New York

Glickstein, Sara Beth (Neuroscience). B.S. 1992, University of Pittsburgh. Sayre, Pennsylvania

Goodman, Diana Marcie (Cell Biology and Genetics). B.A. 1994, University of Pennsylvania. New York, New York

Greenfield, Jeffrey (Neuroscience). B.A. 1994, Amherst College. Brooklyn, New York

Jacovina, Andrew (Biochemistry and Structural Biology). B.S. 1990, State University of New York at Stony Brook. Rockville Center, New York

Jiang, Licong (Biochemistry and Structural Biology). B.S. 1990, Tsinghau University, (People's Republic of China); M.S. 1994, University of Maryland. Fujian, People's Republic of China

Jin, Shengkan (Pharmacology). B.S. 1992, Tsinghua University, (People's Republic of China). Hunan, People's Republic of China

Kim, MeaDou (Pharmacology). Seoul National University, (Korea). Seoul, Korea

Lehman, Kevin Scott (Neuroscience). B.S. 1991, Fordham University. Mt. Vernon, New York

Leu, Frank Pou (Pharmacology). B.A. 1994, State University of New York, Binghamton. Kao-Shihn City, People's Republic of China

Liu, Yan (Neuroscience). M.D. 1985, Shanxi Medical College, (People's Republic of China). Tianjin, People's Republic of China

Loconti, Andrea (Pharmacology). B.S. 1994, University of Syracuse. Potsdam, New York

McAvoy, Thomas Andrew (Pharmacology). B.S. 1993, Virginia Polytechnic Institute and State University. Richmond, Virginia

Meneses, Patricio (Neuroscience). B.S. 1990, State University of New York at Stony Brook. Llay-Llay, Chile

Nguyen, Kha Chi (Neuroscience). B.S./B.A. 1993, University of Rochester. Saigon, Vietnam

Park, Michele (Molecular Biology). A.B. 1994, Princeton University. Niagara Falls, New York

Qiao, Jizeng (Physiology and Biophysics). M.D. 1977, Beijing 2nd Medical College, (People's Republic of China); M.A. 1993, Columbia University. Beijing, People's Republic of China

Safer, Michelle Laurie (Pharmacology). B.A. 1994, Brandeis University. New York, New York

Sinclair, Meeghan (Neuroscience). B.A. 1992, Hunter College. Jersey City, New Jersey

Srethapakdi, Mary (Molecular Biology). B.A. 1993, Cornell University. Bangkok, Thailand

Stebbins, Charles Erec (Biochemistry and Structural Biology). B.S. 1992, Oberlin College. Lincoln, Nebraska

Tritel, Marc (Cell Biology and Genetics). A.B. 1991, Harvard University. Philadelphia, Pennsylvania

Tumang, Joseph (Immunology). B.S. 1994, Regents College. Quezon City, Philippines

Ward, Jeremy Ogden (Cell Biology and Genetics). B.A. 1994, Cornell University. New Haven, Connecticut

Wei, Yan (Cell Biology and Genetics). B.S. 1986, Tsinghua University, (People's Republic of China). Beijing, People's Republic of China

Westman, Sheila (Pharmacology). B.A. 1994, Bard College. San Diego, California

Yu, Lei (Molecular Biology). B.A. 1994, Concordia College. Tianjin, People's Republic of China

Continuing Students

[3]Abraham, Dicky G. (Biochemistry and Structural Biology). M.S. 1987, Indian Institute of Technology. Kuwait City, Kuwait

Allan, Vicki Marie (Cell Biology and Genetics). B.S. 1992, Cook College, Rutgers University. Montclair, New Jersey

Alroy, Iris (Cell Biology and Genetics). B.S. 1989, Tel Aviv University. Tel Aviv, Israel

Altun-Gultekin, Zeynep F. (Neuroscience). M.D. 1985, Istanbul Faculty of Medicine. Trabzon, Turkey

[1]Arnold, James B. (Neuroscience). B.A. 1982, Columbia College. New York, New York

Atherton, Ruth Elizabeth (Cell Biology and Genetics). B.A. 1993, University of California, Santa Barbara. Portland, Oregon.

Baldwin, Michael (Molecular Biology). B.A./B.S. 1993, State University of New York, Binghamton. Massapequa, New York

Bannish, Gregory (Immunology). B.S. 1990, University of Massachusetts, Amherst. Springfield, Massachusetts

Barami, Kaveh (Neuroscience). B.S. 1985, Wright State University; M.D. 1989, University of Cincinnati College of Medicine. United Kingdom

Basu, Subham (Pharmacology). B.A. 1991, University of California, Berkeley. Noamundi, India

Bennett, Richard Lynn (Molecular Biology). B.A. 1993, Kalamazoo College. Detroit, Michigan

Bradsher, John Norman (Molecular Biology). B.S. 1989, Oklahoma Baptist University; M.S. 1990, University of Oklahoma. Broken Arrow, Oklahoma

Brodsky, Marina (Pharmacology). First Degree 1984, Kalinin State University (USSR). Moscow, USSR

Bromleigh, Virginia Carrington (Cell Biology and Genetics). B.A. 1987, M.S. 1990, New York University. Anaheim, California

[3]Brooks, David G. (Molecular Biology). B.A. 1982, University of Colorado; M.S. 1984, Michigan State University. Pontiac, Michigan

Brown, George P. (Neuroscience). B.S. 1990, Fordham University. Worcester, Massachusetts

Byrd, Cynthia Anne (Immunology). B.S. 1993, University of Maryland. Baltimore, Maryland

Cai, Jinsong (Cell Biology and Genetics). B.S. 1989, Sichuan University (People's Republic of China); M.S. 1993, University of Vermont. Shen Yung, P.R. China

Chang, Shang-Yu (Molecular Biology). B.S. 1985, M.S. 1987, National Tsing-Hua University. Taipei, Taiwan, Republic of China

Chen, Bihua (Molecular Biology). B.S. 1990, Fudan University. Zhejiang, People's Republic of China

Chen, Xinyue Liu (Neuroscience). B.A. 1992, Beijing Medical University (People's Republic of China). Beijing, People's Republic of China

Cheng, Jie (Neuroscience). B.M. 1988, Shanghai Medical University. Shanghai, People's Republic of China

Chien, Chih-cheng (Neuroscience). M.B. 1988, National Taiwan University. Chia-Yi, Taiwan, Republic of China

Chittka, Alexandra Nedlin (Neuroscience). B.A. 1985, Grinnell College. Leningrad, U.S.S.R.

Cho, Hearn (Immunology). A.B. 1988, Princeton University. Las Vegas, Nevada

Chung, Sangmi (Neuroscience). B.S. 1993, Seoul National University. Seoul, Korea

Circle, David A. (Biochemistry and Structural Biology). B.S. 1990, University of Georgia. Marietta, Georgia

Commons, Kathryn G. (Neuroscience). B.S. 1989, Hofstra University. Port Washington, New York

Cong, Peijie (Molecular Biology). B.S. 1984, The Fourth Army Medical College; M.S. 1987, Institute of Radiation Medicine. Shandong, People's Republic of China

Cram, Jody Catherine (Neuroscience). B.S. 1992, University of California, San Diego. Minneapolis, Minnesota

Crombie, Andrea Rene (Molecular Biology). B.A. 1981, Groucher College. San Diego, California

Das, Indranil (Neuroscience). B.A. 1993, Northwestern University. Calcutta, India

Deng, Liang (Cell Biology and Genetics). B.S. 1991, University of Rochester. Huzhou City, People's Republic of China

de Silva, Heshani Eranthi (Cell Biology and Genetics). A.B. 1992, Mount Holyoke College. Sri Lanka

Ding, Xiao-Hong (Molecular Biology). B.S. 1984, Shanghai Medical University; M.S. 1988, Shanghai Institute of Materia Medica, Chinese Academy of Sciences. Hangzhou, People's Republic of China

Djokic, Miroslav (Molecular Biology). B.A. 1987, City College of the City University of New York; Diploma 1992, Faculty of Medicine of the University of Belgrade. Belgrade, Yugoslavia

Donovan, Gerald Patrick (Pharmacology). B.S. 1993, University of California, Davis. Sacramento, California

Du, Shan (Cell Biology and Genetics). B.S. 1984, M.S. 1987, Peking University. Chengdu, People's Republic of China

Dumitru, Calin Dan (Immunology). M.D. 1989, University of Medicine and Pharmacy (Romania). Iasi, Romania

Dyall, Rubendra (Immunology). B.Sc., M.Sc. 1988, School of Medicine, University of Bordeaux II (France). Mauritius

Egan, David A. (Neuroscience). B.Sc. 1991, University of Limerick (Ireland). Limerick, Ireland

Einarson, Margaret (Molecular Biology). B.S. 1988, Bates College. New York, New York

Erçikan, Emine A. (Pharmacology). B.S. 1986, M.S. 1988, University of Southwestern Louisiana. Nicosia, Cyprus

Eubanks, Sharon Kay (Biochemistry and Structural Biology). B.S. 1980, University of Redlands. Ft. Leavenworth, Kansas

Fan, Wen (Immunology). B.S. 1990, Beijing Medical University (People's Republic of China). Xian, People's Republic of China

Fang, Linhua (Molecular Biology). B.S. 1985, Zhejiang Medical University; M.S. 1989, Peking Union Medical College. Zhejiang, People's Republic of China

Ferguson, David (Molecular Biology). B.S. 1988, University of Rochester. New York, New York

Flores-Rozas, Hernan (Molecular Biology). B.A. 1987, M.S. 1989, University of Concepcion. Valparaiso, Chile

Folger, Paula A. (Cell Biology and Genetics). B.A. 1986, University of California at Santa Cruz. Pawtucket, Rhode Island

Ford, Renee D. (Cell Biology and Genetics). B.S. 1989, Simmons College. Sanford, Maine

[2]Fratangelo, Peter (Molecular Biology). B.S. 1993, Tufts University. New York, New York

Gall, Jason Graham David (Molecular Biology). B.S. 1990, M.S. 1992, University of California, Davis. Davis, California

Gannon, Maureen (Cell Biology and Genetics). B.S. 1985, Molloy College; M.S. 1988, Adelphi University. Queens, New York

Garepapaghi, Mohammad A. (Physiology and Biophysics). B.A. 1987, Bowdoin College of Maine. Meiandoab, Iran

Giarre, Marianna (Cell Biology and Genetics). B.S. 1987, M.S. 1989, University of Geneva (Switzerland). Araraquara, Brazil

Gibbs, Emma E. (Molecular Biology). B.Sc. 1988, M.Sc. 1991, University of Auckland (New Zealand). Auckland, New Zealand

Gracy, Kimberly Noelle (Neuroscience). B.A. 1992, The University of Texas at Austin. Denton, Texas

Gu, Chengua (Cell Biology & Genetics). B.S. 1991, Beijing Agricultural University (People's Republic of China), M.S. 1993, Rutgers University. Beijing, People's Republic of China

Guger, Kathleen Ann (Cell Biology and Genetics). B.S. 1992, Carnegie-Mellon University. Pittsburgh, Pennsylvania

Güre, Ali (Immunology). M.D. 1988, University of Ankara. Ankara, Turkey

[3]Halaby, Issam (Neuroscience). B.S. 1987, American University of Beirut. Beirut, Lebanon

[1]Han, Jihong (Biochemistry and Structural Biology). B.S. 1987, M.S. 1989, Nankai University. Anhui Province, People's Republic of China

Hatini, Victor (Molecular Biology). B.A. 1989, The Hebrew University of Jerusalem (Israel); M.Sc. 1991, The Weizmann Institute of Science (Israel). Jerusalem, Israel

Heyrovská, Neela (Molecular Biology). B.Sc. 1990, M.Sc. 1992, Faculty of Natural Sciences, Charles University (Czechoslovakia). Prague, Czechoslovakia

Ho, Chong-Kiong (Molecular Biology). B.A. 1990, Rutgers University. Yokohama, Japan

Hoffman, Mary M. (Pharmacology). B.S. 1989, Ithaca College; M.S. 1992, Bucknell University. Bronx, New York

Hom, Judith Seuk Han (Pharmacology). B.S. 1990, Cornell University. New York, New York

Huh, Ho Young (Cell Biology and Genetics). B.A. 1992, Dartmouth College. Seoul, Korea

Hyer, Jeanette D. (Cell Biology and Genetics). B.S. 1991, University of Connecticut. Massapequa, New York

Ince, Tan (Pharmacology). M.D. 1988, Hacettepe University of Medicine. Aydin, Turkey

Jen, Yale I-E. (Molecular Biology). B.S. 1979, National Taiwan University; M.S. 1982, Louisiana State University. Taipei, Taiwan, Republic of China

Jin, Fen Yu (Immunology). B.M. 1990, Beijing Medical University (P.R. China). Beijing, People's Republic of China

Kelman, Zvi, (Molecular Biology). B.Sc. 1987, The Hebrew University of Jerusalem (Israel); M.Sc. 1989, The Weizmann Institute of Science (Israel). Haifa, Israel

Kim, Karl H.S. (Neuroscience). B.S. 1989, Michigan State University. Seoul, Korea

Kim, Sung Sub (Molecular Biology). B.S. 1986, M.S. 1988, Seoul National University. Seoul, Korea

Kuhlman, Julie Ann (Cell Biology and Genetics). B.Sc. 1989, University of Illinois at Urbana-Champaign. Ecket, Nigeria

Lee, Cynthia Ellen (Pharmacology). B.S. 1991, College of William and Mary. Washington, D.C.

[1]Lee, Seong-Wook (Molecular Biology). B.S. 1985, M.S. 1987, Seoul National University. Seoul, Korea

Le Gall, Annick H. (Cell Biology and Genetics). B.S. 1990, University of California, Los Angeles. Palo Alto, California

Lemon, Bryan D. (Molecular Biology). B.S. 1991, University of Delaware. Havre de Grace, Maryland

Levine, Cindy (Molecular Biology). B.S. 1990, Cornell University. Oceanside, New York

Li, Bibo (Physiology and Biophysics). B.S. 1990, Peking University. Beijing, People's Republic of China

Li, Dangsheng (Molecular Biology). B.S. 1988, University of Science and

Technology of China. Yan Chen City, People's Republic of China

Li, Hailong (Molecular Biology). B.S. 1987, Beijing University. Beijing, People's Republic of China

Li, Tao (Immunology), B.S. 1988, Beijing Normal University; Hunan Province, People's Republic of China

Li, Yong (Molecular Biology). Beijing, People's Republic of China

Liang, Feng (Molecular Biology). B.S. 1988, Peking University. Jinan, People's Republic of China

Ling, Tao Tao (Biochemistry and Structural Biology). B.S. 1989, M.S. 1992, Peking University (People's Republic of China). Harbin, People's Republic of China

Liu, Cheng (Molecular Biology). B.S. 1982, Peking University; M.S. 1985, Capital Institute of Medicine. Tiao Zhou City, People's Republic of China

Liu, Franklin (Molecular Biology). B.A. 1993, Colgate University. New Brunswick, New Jersey

Liu, Jiong (Neuroscience). B.S. 1992, Rutgers University. Shanghai, People's Republic of China

Liu, Ke (Molecular Biology). B.M. 1984, Henan Medical University; M.M. 1988, National Institute for the Control of Pharmaceutical and Biological Products. Neixiang, People's Republic of China

Liu, Min (Pharmacology). B.S. 1985, M.S. 1988, Zhongshan University. Guangzhou, People's Republic of China

[2]Liu, Qing (Biochemistry and Structural Biology). B.S. 1986, Nankai University. Tianjin, People's Republic of China

Luz, John Gately (Pharmacology). B.A. 1991, Berklee College of Music; B.S. 1993, University of Massachusetts. Brighton, Massachusetts

MacMicking, John (Immunology). B.S. 1991, Australian National University. Temora, Australia

Maer, Andreia Mirela (Physiology and Biophysics). B.S. 1992, M.S. 1993, University of Bucharest (Romania). New York, New York

[3]Manley, Geoffrey (Neuroscience). B.S. 1988, University of Kentucky. Lexington, Kentucky

Mao, Xiangdong (Molecular Biology). B.S. 1990, Fudan University. Huzhou, People's Republic of China

Mao, Buqing (Neuroscience). B.E. 1985, M.M. 1988, Shanghai Medical University. Shanghai, People's Republic of China

[3]Mayer, Alan (Molecular Biology). B.S. 1986, M.S. 1986, Emory University. Passaic, New Jersey

Mennitt, Patricia Anne (Physiology and Biophysics). B.S. 1987, Alfred University; B.S.N. 1991, M.S.N. 1993, University of Virginia. Brooklyn, New York

Molano, Alberto (Immunology). M.D. 1988, Colegio Mayor de Nuestra Señora del Rosario, School of Medicine (Colombia). Bogotá, Colombia

Nachman-Clewner, Michele (Neuroscience). B.Sc. 1989, The Hebrew University of Jerusalem (Israel). New York, New York

Neel, Olivia Davis (Biochemistry and Structural Biology). B.A. 1990, St. John College. New York, New York

Netzer, William J. (Immunology). B.S. 1971, Brooklyn College. Brooklyn, New York

Newberger, Carol Lynn (Biochemistry and Structural Biology). B.A. 1979, Pomona College, Honolulu, Hawaii

Ng, Yik-Bing Jenny (Molecular Biology). B.Sc. 1987, University of Calgary (Canada). Hong Kong

Nirenberg, Melissa J. (Pharmacology). B.A. 1990, Yale University. Brooklyn, New York

Niu, Hongwu (Molecular Biology), B.S. 1988, M.A. 1991, Peking University. Shanghai, People's Republic of China

Noramly, Selina (Molecular Biology). B.A. 1992, St. Hilda's College, Oxford University (United Kingdom). Kuala Lumpur, Malaysia

Onel, Kenan (Neuroscience). B.S. 1984, M.A. 1985, Yale University. Scarsdale, New York

Ouyang, Honghai (Physiology and Biophysics). B.S. 1988, East China University of Chemical Technology. Changsha, People's Republic of China

Packer, Alan (Cell Biology and Genetics). B.A. 1988, Brandeis University. New Hyde Park, New York

[2]Paik, John (Immunology). B.A. 1990, University of Pennsylvania. Providence, Rhode Island

Pambuccian, Corina Alice (Immunology). Diploma de Bacalaureat 1977, C. Brediceanu Lyceum; M.D. 1983, University of Bucharest Medical School (Romania). Lugoj, Romania

Peng, Hong (Molecular Biology). B.S. 1982, M.S. 1985, Institute of Zoology, Academia Sinica. Beijing, People's Republic of China

Peng, Yufeng (Biochemistry and Structural Biology). B.S. 1993, University of Science and Technology of China (People's Republic of China). Chang Sha, People's Republic of China

[1]Pinto, Shirley (Neuroscience). B.A. 1988, M.S. 1992, New York University. Haifa, Israel

Polyak, Kornelia (Molecular Biology). M.D. 1991, Albert Szent-Györgyi Medical University (Hungary). Jaszbereny, Hungary

Ponomareff, Gregory (Molecular Biology). B.A. 1988, University of California, San Diego. Oakland, California

[3]Ramakrishna, Naren R. (Cell Biology and Genetics). B.A. 1985, Johns Hopkins University. Bangalore, India

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[1] in absentia
[2] leave of absence
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